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ABSTRACTS OF WORLD MEDICINE

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ABSTRACTS OF WORLD MEDICINE

This journal is planned to provide the reader with a selection of abstracts of the more important articles appearing in medical periodicals published in different parts of the world. Comment by the abstracter, when thought necessary, is inserted between square brackets, usually at the end of an abstract. In some instances only the titles of articles are provided.

The titles of journals are given in full and also abbreviated according to the rules adopted in the *World List of Scientific Periodicals* and in *World Medical Periodicals*. The titles of articles from foreign journals are translated into English.

This journal is essentially a guide to work in progress in the world's medical centres. No abstract can be regarded as a substitute for the article abstracted. For complete information the original article must be consulted. Our aim is to give the reader sufficient details in an abstract to enable him to judge whether the original is, for him, worth reading in full.

The abstracts are grouped in broad classifications and, so far as possible, those dealing with medical and surgical aspects of the same problem appear together under the same heading. The specialist will, it is hoped, learn from this journal of work done in other fields as well as in his own. The general practitioner will be able to keep abreast of modern knowledge in the various specialties. The representation in one journal of the several aspects of Medicine will, it is believed, give an integrated picture of the whole, necessary in this age of specialization.

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Pathology

EXPERIMENTAL PATHOLOGY

1481. **A Histological and Histochemical Study of Granulation Tissue under the Influence of Tissue Therapy. Comparison with the Action of Cortisone.** (Étude histologique et histochimique du tissu de granulation sous l'influence de la thérapeutique tissulaire. Comparaison avec l'action de la cortisone)
R. DU BOISTESSELIN and J. DE BRUX. *Presse médicale*, [*Presse méd.*] **61**, 543–545, April 15, 1953. 3 figs., 14 refs.

Although there have been many reports of the clinical effects of Filatov's tissue therapy, there have been few histochemical studies. In this study, carried out in the Department of Pathological Anatomy, Hôpital Boucicaut, Paris, two groups of male white rats received implants of an inert material (" spongel ") under the muscular wall of the abdomen, the second group being given in addition three injections of 25 mg. of cortisone in the course of one week; in a third group of animals the implant consisted of dried placenta. One animal from each group was then killed each week and the implants were investigated macroscopically and microscopically, specific stains for collagen, reticulin, amyloid, mucoid, and mucopolysaccharides being employed. The testicles and adrenal glands were also examined.

There was no hard fibrous tissue around the implant in the animals given cortisone, or in the group receiving the implant of placental tissue, the two groups differing only in that the placental implants produced more blood vessels and, histochemically, a high concentration of mucopolysaccharides. In the cortisone-treated group the adrenal glands showed cortical atrophy, but in none of the three groups was there a change in the testicles. The authors suggest that placental tissue contains a principle which activates the proliferation of fibroblasts.

H. Lehmann

1482. **Studies on Entry and Egress of Poliomyelitic Infection. VI. Centrifugal Spread of the Virus into Peripheral Nerve: with Notes on its Possible Implications**
H. K. FABER, R. J. SILVERBERG, and L. DONG. *Journal of Experimental Medicine* [*J. exp. Med.*] **97**, 455–465, March, 1953. 27 refs.

The centrifugal spread of the poliomyelitis virus from the central nervous system (C.N.S.) into the peripheral nervous system was studied at Stanford University, San Francisco. Cynomolgus monkeys were infected with poliomyelitis virus in two ways: (1) by applying a virus suspension to the cut sciatic nerve on the left side; and (2) by intrathalamic injection.

The results are claimed to demonstrate a progressive centrifugal migration of virus from the C.N.S. into various peripheral ganglia and peripheral nerves, including their distal portions. Viraemia appeared to be secondary to primary neural infection. The presence of virus in the lumen of the gut was thought to result from neural spread and not from viraemia. It is suggested that the presence of the virus in " extraneural " tissues may be due to infection of the nerves supplying the constituent cells or to their content of virus-infected blood, rather than to infection of the constituent cells themselves. The presence of virus in peripheral nerves is considered to be a possible cause of the localized pain and tenderness observed in poliomyelitis in human beings.

Peter Story

1483. **The Action of Flint of Variable Size Injected at Constant Weight and Constant Surface into the Lungs of Rats**
E. J. KING, G. P. MOHANTY, C. V. HARRISON, and G. NAGELSCHMIDT. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **10**, 76–92, April, 1953. 31 figs., 11 refs.

This paper describes an experimental investigation, carried out at the Postgraduate Medical School, London, and the Safety in Mines Research Establishment, Sheffield, into the relation of particle size to the toxicity of quartz dust on injection into the lungs of rats. Ground calcined flint (99% free silica) containing quartz (50%) and cristobalite (35 to 45%) was separated by sedimentation and centrifugation into five fractions with size ranges of less than 0·5 μ, 0·5 to 1 μ, 1 to 2 μ, 2 to 4 μ, and 4 to 8 μ (equivalent spherical diameter) respectively. The proportions of quartz and cristobalite were the same in the different fractions.

To compare the effects of equal masses of the different sized dusts, 15 ml. of a suspension in saline of each, containing 50 mg. of dust, was injected intratracheally into rats by open operation, during which some regurgitation of the suspension occurred. To compare the effects of varying mass with constant surface the doses of the various fractions injected were such as were calculated to have an equivalent surface area (700 sq. cm.). (Electron microscopy of the finest fraction later showed that its surface had been overestimated, and that the surface area of the dose injected was only 520 sq. cm.). The quantity of dust in the larger size ranges was too

great for a single injection and had to be given in 2 to 4 injections at weekly intervals. Peroral injection was substituted for intratracheal in this series, and no dust was lost by regurgitation. Rats were killed at monthly intervals up to one year in the first series and 500 days in the second, a large number being lost by death and cannibalism in the former. The degree of fibrosis present in the lungs was graded 1 to 5 according to the system proposed by Belt and King (*Spec. Rep. Ser. med. Res. Coun. (Lond.)*, 1945, No. 250, 29) which is based on the number, size, and maturity of the silicotic nodules. The results are shown in the following tables:

CONSTANT MASS (50 mg.)

Flint Size (μ)	Silica Solubility (mg./100 ml.)	Surface per Rat (sq. cm.)	Maximum Stage of Fibrosis	Reached after Months	Minimum Time (Months) to Give Stage			
					2	3	4	5
4–8	5·1	170	2	9	9	—	—	—
2–4	8·9	350	3	10	5	10	—	—
1–2	13·1	750	5	9	1	5	7	9
0·5–1	13·4	2,000	5	7	1	2	3	7
<0·5	13·6	3,000	5	5	<1	<1	1	5

CONSTANT SURFACE (700 sq. cm.)

Flint Size (μ)	Weight of Dust per Rat (mg.)	Minimum Time (Months) to give Fibrosis Stage		
		3	4	5
4–8	199	8	—	—
2–4	100	1	4	6
1–2	42	1	4	5
0·5–1	17·5	1	7	10
<0·5*	8	1	10	—

* This sample represents 520 sq. cm.

Whether or not silica acts on the lung through the action of dissolved silicic acid, it would be expected that its action would be determined by the total surface of the particles administered rather than by their mass. It will be seen that in the "constant-mass" series there is a regular and large increase in fibrogenic activity as the particle size diminishes and the total surface increases. The " constant-surface " series suggests that fibrogenic activity is greatest with a particle size of 1 to 2 μ and that larger and smaller sizes are less active. The larger size fractions may have been less fibrogenic because of the smaller number of particles, but that cannot explain the relatively small effect of the smallest size range. It is possible that this is due to complete solution of the finest particles before sufficient time has elapsed for Stage-5 fibrosis to develop. *C. M. Fletcher*

1484. **Endocrine Factors in Experimental Renal Hypertension**

R. W. SEVY and G. E. WAKERLIN. *American Journal of Physiology* [*Amer. J. Physiol.*] **172**, 129–140, Jan., 1953. 41 refs.

The effect of a number of endocrine preparations on experimental renal hypertension in dogs was studied by the authors at the University of Illinois College of Medicine, Chicago. Crude beef anterior pituitary extract was found to exert an antihypertensive effect, particularly after repeated courses of treatment extending over several months had been given. Corticotrophin (ACTH) was present in the extract and may have been the active principle, although purified corticotrophin was not so effective as the crude extract. Changes in the renal clearances of creatinine and *p*-aminohippurate were not correlated with the antihypertensive effect, and no evidence was found of any alteration in pituitary–adrenal function in experimental renal hypertension. The adrenal ascorbic acid level was reduced in normal rats on administration of renin, but not in hypophysectomized rats, which suggests that renin stimulates the pituitary–adrenal system. Administration of deoxycortone acetate lowered the renal renin concentration in dogs without causing a detectable increase in renin secretion, but did not prevent the development of experimental renal hypertension. *F. W. Chattaway*

CHEMICAL PATHOLOGY

1485. **The Interpretation of Fractional Test Meals: Some Studies in a " Glass Stomach "**

J. N. HUNT. *Guy's Hospital Reports* [*Guy's Hosp. Rep.*] **102**, 157–163, 1953. 5 figs., 5 refs.

In experiments carried out at Guy's Hospital, London, 0·752 N hydrochloric acid, corresponding to the maximum concentration likely to be found in the gastric secretion, was added at a constant rate to 750 ml. of water in a glass tank with a siphon so designed as to empty it at a constant rate of 3·3% of its contents per minute. (The author refers to previous experiments (*J. Physiol.*, 1951, **113**, 157 and 169) in which the mean emptying pattern of the human stomach was shown to be of similar exponential form.) As in the standard test meal, samples were taken at 10-minute intervals and the acidity determined; the effect on the acidity of changes in the emptying rate and in the rate at which acid was added is shown graphically. No attempt was made to imitate the normal falling-off in the rate of gastric secretion in the course of a test meal; hence all the curves show a steady increase in acidity, but they nevertheless serve to demonstrate the fact that doubling the emptying rate has the same effect on the acidity of the contents as doubling the rate at which acid is added, and to emphasize yet once more that a test meal is useless as a measure of the secretory activity of the stomach.

Denys Jennings

1486. **Serum Mucoprotein Level in Differentiation of Hepatogenic from Obstructive Jaundice**

E. M. GREENSPAN and D. A. DREILING. *Archives of Internal Medicine* [*Arch. intern. Med.*] **91**, 474–486, April, 1953. 7 figs., 22 refs.

The authors have studied the serum mucoprotein concentrations in healthy subjects and in patients with various diseases of the liver and biliary tract at the U.S. National Cancer Institute and Mount Sinai Hospital, New York. The ranges of mucoprotein concentration in 185 healthy men and women were from 48 to 75 mg. and from 40 to 70 mg. per 100 ml. respectively. The

first serum sample from 180 patients with infective or homologous serum hepatitis or portal cirrhosis showed a reduced mucoprotein concentration in 88% of cases, and this percentage would have been greater if patients with coexistent disease not affecting the liver had been excluded. In 8 patients with fatty infiltration of the liver (proved by biopsy) the serum mucoprotein levels were within the normal range. Of 11 patients with infectious mononucleosis and positive heterophile tests, the mucoprotein level was increased in 5, normal in 5, and reduced in one who had severe jaundice. Only 3 of 125 patients with obstruction of the biliary tract showed reduced mucoprotein concentration, regardless of the cause of the obstruction. In this group raised mucoprotein levels were found more commonly in cases of acute inflammation of the biliary tract and gall-bladder than in cases of well-localized or early malignant tumour producing obstruction. In none of 7 patients with biliary cirrhosis was the mucoprotein concentration low, in spite of marked secondary pathological changes in the liver. The serum mucoprotein levels were raised in 50 out of 52 patients with hepatomegaly due to metastases in the liver, while of 48 patients with hepatomegaly due to lymphoma or leukaemia the serum mucoprotein concentration was raised in 41, was normal in 3, and reduced in 4. In 3 of these 4 patients with low mucoprotein values jaundice developed " after treatment with antineoplastic drugs ", and at necropsy the liver showed parenchymatous degeneration but no metastatic invasion.

Increased mucoprotein values were encountered in 22 of 31 patients with congestive heart failure of varied aetiology; of the remainder, the level was normal in 6, and reduced in 3. The incidence of occurrence of a low serum mucoprotein concentration equalled or exceeded the incidence of abnormal results in serum globulin and alkaline phosphatase estimations, in the cephalin flocculation, thymol turbidity, and zinc sulphate turbidity tests, and also in estimations of prothrombin time in all cases of parenchymatous liver disease. In obstructive jaundice, on the other hand, there was 'a very low incidence of false positive results (that is, of low serum concentrations). Only the estimation of alkaline phosphatase concentration and the cephalin flocculation test approached the estimation of serum mucoprotein concentration in value as differential diagnostic tests of obstructive and parenchymatous liver disease. The results of serial mucoprotein determinations and the physiological significances of the fluctuations encountered are discussed.

Walter H. H. Merivale

1487. **The Assessment of Liver Function from Variations in the Faecal Stercobilin Content.** (Contrôle de la fonction biliaire par les variations de la stercobiline)
R. CATTAN, O. GAUDIN, and J. BATAILLE. *Presse médicale* [*Presse méd.*] **61,** 521–522, April 11, 1953. 2 figs., 12 refs.

The faecal content of stercobilin, which is derived from bilirubin by reduction and oxidation, is thought to provide an accurate index of the amount of bile produced by the liver. The faecal excretion of stercobilin by 20 patients was therefore measured by the method of Watson *et al.* (*Amer. J. clin. Path.*, 1944, **14,** 598) for a 4-day period before and after the daily administration for 8 to 10 days of 75 mg. of a new anhydrous choleretic, trithio*para*methoxyphenylpropene.

In 4 of the patients, who had no liver disease, there was only a slight increase (about 10%) in stercobilin excretion, but in the 16 patients with hepatic disorder there was a much greater increase (from 35 to 490%). The test thus permits changes in choleresis to be followed, and it may also be useful in diagnosis. The method is claimed to be simple to carry out and to give accurate results.

J. E. Page

1488. **Relationship between Potassium and Bicarbonate in Blood and Urine**
K. E. ROBERTS, M. G. MAGIDA, and R. F. PITTS. *American Journal of Physiology* [*Amer. J. Physiol.*] **172,** 47–54, Jan., 1953. 2 figs., 37 refs.

An account is given of 18 experiments on 7 mongrel bitches at Cornell University Medical College, New York. Following adequate control periods the animals received infusions from a calibrated pump of potassium chloride (0·67 to 1·0 mEq. per minute) or sodium bicarbonate (0·6 to 2·0 mEq. per minute). The effects of the administration of these solutions on the plasma concentration and urinary excretion of bicarbonate, sodium, and potassium and on the urinary *p*H and titratable acid excretion were assessed over a period of 4 to 5 hours.

The infusion of potassium chloride was found to produce a fall in plasma *p*H and bicarbonate concentration as well as a concomitant rise in urinary *p*H accompanied by an increased excretion of bicarbonate. In 2 further experiments small amounts of potassium chloride were administered to an animal receiving a continuous infusion of buffered sodium phosphate solution. In spite of the urine being highly buffered and containing considerable amounts of phosphate, there was an increase in the excretion of bicarbonate, elevation of the urinary *p*H, and a fall in the rate of excretion of titratable acid. The infusion of sodium bicarbonate led to a rise in plasma bicarbonate concentration, accompanied by a simultaneous fall in plasma potassium value. There was an increase in potassium excretion despite a decrease in the plasma concentration of this ion.

The effects of potassium chloride infusion are explained in part by increased excretion of bicarbonate, but mainly by ion transfers, chloride being retained in the extracellular compartment, whereas potassium, with equivalent quantities of bicarbonate, is transferred into the cells. These ion transfers lead to extracellular acidosis and intracellular alkalosis. It is suggested that such hyperkalaemia and alkalinization occurring in the renal tubular cells may affect their function in the direction of reduction in the exchange of cellular hydrogen ions for sodium ions and its replacement by an exchange of potassium for sodium, with consequent alkalinization of the urine.

It is stressed that the clinical syndrome of hypochloraemic alkalosis with hypokalaemia is not equivalent to the conditions produced by the experimental procedures described in this paper.

A. Swan

1489. **An Improved Test for Bilirubin in Urine**
G. KLATSKIN and L. BUNGARDS. *New England Journal of Medicine* [*New Engl. J. Med.*] **248**, 712–717, April 23, 1953. 3 figs., 17 refs.

The specificity and sensitivity of Free and Free's diazo mat test for bilirubin in urine (*Proceedings of the 122nd Meeting of the American Chemical Society*, 1952) were examined at Yale University School of Medicine. In this test 5 drops of urine are placed on an absorbent cellulose–asbestos mat; a tablet containing *p*-nitrobenzene diazonium *p*-toluene sulphonate, sodium bicarbonate, sulphosalicylic acid, and boric acid is placed on the moist area and the tablet flooded with 2 drops of water. The appearance of a blue or purple colour within 30 seconds indicates the presence of bilirubin. [The quantitative composition of the tablet (the " ictotest " tablet) is not given.] The test detected a concentration of bilirubin as low as 0·05 mg. per 100 ml. of urine, and was more sensitive than the tests of Sparkman, of Watson and Hawkinson, and of Franklin, with all three of which it was compared. With 0·4% false positive reactions in 478 tests it was also more specific than Sparkman's test (2·0% false positive reactions in 1,343 tests). The Watson–Hawkinson and Franklin tests gave no false positive reactions among 847 and 842 tests respectively. The unique simplicity, sensitivity, and specificity of the Free test are emphasized. *J. E. Page*

MORBID ANATOMY AND CYTOLOGY

1490. **The Role of the Lymphatics in the Development of Bronchogenic Tuberculosis**
P. SCHWARTZ. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **67**, 440–452, April, 1953. 5 figs., bibliography.

Extensive investigations carried out at necropsy in cases of tuberculosis at Istanbul University revealed that lymph-node perforation occurred in 90% of lungs affected by active tuberculosis. In the majority of cases the perforation caused inflammatory consolidation in the parenchymal sector supplied by the involved bronchus. In the author's view tuberculosis is a lymph-node disease, and the infiltrations and destructive processes seen in the lung are secondary to perforation of the bronchi by tuberculous lymph nodes.

R. Heptinstall

1491. **The Bronchopulmonary Venous Collateral Circulation with Special Reference to Emphysema**
A. A. LIEBOW. *American Journal of Pathology* [*Amer. J. Path.*] **29**, 251–289, March–April, 1953. 26 figs., 25 refs.

The venous circulation of the lung in health and disease has been studied by the author at Yale University School of Medicine, vinylite casts of the veins draining the bronchial tree being obtained by retrograde injection from the left auricle and azygos vein. The technique [for details of which the original article should be consulted] was a modification of that previously described by the author and others (*J. techn. Meth.*, 1947, **27**, 116). In 65 normal lungs the findings of earlier workers were confirmed—namely, that the venules in the walls of the more peripheral bronchi and bronchioles drain principally into the pulmonary veins, while the venous plexus surrounding the more central bronchi drains principally into the azygos system, there being a number of demonstrable anastomoses between the latter group and the major pulmonary veins. Communications between the more peripheral venous system and the veins draining into the azygos vein or its branches could not be demonstrated owing to the viscosity of the vinylite, but such connexions are commonly found in certain diseases in which expansion of the venous system occurs and are probably present in the healthy lung, if only at capillary level. In view of their intimate intercommunication with the pulmonary veins, all vessels draining the bronchi and bronchioles are designated " bronchopulmonary " by the author.

The collateral venous drainage thus provided by the bronchopulmonary veins was greatly increased in 7 cases of advanced emphysema studied, constituting a shunt of considerable size between the two sides of the heart. The direction of flow in such cases is probably usually from left to right, but may become reversed when, as a result of venous dilatation, the valves between the bronchopulmonary and azygos veins become incompetent. In the cases of emphysema, expansion of the bronchopulmonary venous collateral circulation accompanied a similar increase in the arterial collateral circulation through anastomotic connexions between the pulmonary and bronchial arteries. That this is not necessarily always the case, however, was demonstrated in 12 specimens from cases of bronchiectasis, only one of which showed a notable increase in the venous collateral circulation despite the presence of moderately or markedly increased arterial collateral circulation, and in 11 cases of pulmonary tuberculosis and one of lung abscess, in which the findings were similar. The possible mechanism of the vascular changes is discussed.

G. J. Cunningham

1492. **Milk-aspiration Pneumonia in Human and Animal Subjects**
T. J. MORAN. *Archives of Pathology* [*Arch. Path. (Chicago)*] **55**, 286–301, April, 1953. 8 figs., 7 refs.

The nature of milk-aspiration pneumonia in man and animals has been studied at the St. Margaret Memorial Hospital (University of Pittsburgh). The condition was observed at necropsy on 3 infants and 2 adults, the changes in the lung including acute pneumonia, abscess formation, focal and widespread granulomata, alveolar thickening, giant-cell reaction, and fibrosis. It is pointed out that microscopically the reaction is usually mononuclear and granulomatous at the time of death; giant-cell reaction is not constant and may be absent.

In animal experiments on rabbits varying amounts of human milk, cow's milk, and a milk mixture made from evaporated milk, " dextrimaltose ", and water, were injected into the trachea. The tissue reaction was the same with all three types of milk and was similar to that

seen in human beings. However, more than 10 ml. of the milk mixture often caused death in 1 to 11 minutes, whereas cow's milk or human milk rarely caused death. Microscopically, a reaction to the milk occurred within a few minutes of its injection, and consisted in exudation of erythrocytes, granulocytes, and macrophages, some of which contained fat globules. The late reactions were similar to those seen in the human cases. Although the reaction in both animals and human beings resembled certain features of lipoid pneumonia caused by oils, the general reaction more closely resembled that observed after aspiration of solid foods; this, the author considers, is because the protein in the milk causes a reaction as well as the fat. He emphasizes the difficulty of recognizing milk-aspiration pneumonia, but suggests that in many cases mononuclear pneumonia in infants is due to aspiration of milk. *R. F. Jennison*

1493. **Examination of Pleural Fluid for Carcinoma Cells**
G. G. GRAHAM, J. R. MCDONALD, O. T. CLAGETT, and H. W. SCHMIDT. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **25**, 366–370, April, 1953. 7 refs.

With the object of determining the value of examination of the pleural fluid in suspected cases of primary bronchogenic carcinoma, 418 specimens of pleural fluid from 333 such cases were examined, by the smear technique of McDonald and Broders, at the Mayo Clinic between January, 1947, and February, 1952. Carcinoma cells were found in 112 of these cases, at the first examination in 88 and at the second in 24. The specific type of neoplasm was diagnosed on cell pattern alone in 9 cases. Only one false positive result was observed. Bronchogenic carcinoma was the primary aetiological factor in 56 of these 112 cases. In 114 of the 221 cases in which no carcinoma cells were found the pleural effusion was due to metastatic carcinoma, the primary growth in 47 of these being in the lungs. Operation was possible in only one of the 56 cases of bronchogenic carcinoma in which malignant cells were found and in 2 of the 47 in which the presence of carcinoma cells could not be demonstrated. *Marjorie Le Vay*

1494. **The Histogenesis of Primary Tumours of the Serous Membranes.** (О гистогенезе первичных опухолей серозных оболочек)
D. I. GOLOVIN. *Архив Патологии* [*Arkh. Patol.*] 15, 38–44, March–April, 1953. 5 figs., 23 refs.

The author describes 7 cases of tumour of the pleura, in all of which the neoplasm was regarded as a primary mesothelioma. The tumours developed in one or in both layers of the pleura and spread along the surface of the serous membranes, either as a continuous sheet or focally. In no case was a tumour that could be regarded as a primary origin of metastases found in the bronchi or in any other organ. Four types of structure were observed in these tumours: (1) solid strands and alveolar structures; (2) gland-like cystic structures; (3) isolated polymorphous cells; and (4) elongated fibroblast-like cells. The author points out the considerable similarity between these neoplastic structures of mesothelioma in man and the chronic inflammatory lesions developing during the experimental production of "fibrosing serositis" in frogs and rabbits, and suggests that they exemplify the multiple potentialities of mesothelial cells. *A. Swan*

1495. **Pathogenesis of Coronary Sclerosis**
P. H. LOBER. *Archives of Pathology* [*Arch. Path. (Chicago)*] **55**, 357–383, May, 1953. 8 figs., bibliography.

After reviewing the literature concerning the pathogenesis of coronary sclerosis, and particularly that relating to the influence of sex on its incidence, the author describes an investigation carried out at the University of Minnesota in which the coronary arteries of 536 hearts from subjects of all age groups were studied at necropsy. The hearts were selected at random except that efforts were made to obtain adequate numbers from younger subjects and persons killed accidentally. The coronary arteries were sectioned at 2-mm. intervals, and at that point in each major branch where there was the greatest macroscopic sclerosis a block was taken, its position being recorded by measurement from the orifice.

On histological examination the severity of the atherosclerosis in each of the three major arterial branches, as indicated by the degree of infiltration of the intima, was graded from 0 to 4, these three figures added together giving a total grading for each case, and the degree of degeneration of the internal elastic lamella was similarly graded. In addition, the area of the arterial lumen expressed as a percentage of the entire cross-sectional area, the thickness of the intima expressed as a fraction of the thickness of the entire wall, and the average outside diameter of each arterial section measured in millimetres were recorded as the average for the three vessels in each case. Of the 536 hearts, 314 were from males and 222 from females. The subjects were divided into 10-year age groups, with separate groups for infants up to 1 month and for infants from 1 to 12 months.

The degree of coronary atherosclerosis present, as measured by each of these methods, showed a progressive increase with age and was greater in the males than in the females in every age group, though in the younger groups the difference was not always statistically significant. As a control group, the 83 males and 55 females who had died violently or after a short illness unrelated to cardiovascular disease were studied separately, but the degree of coronary sclerosis was the same in each age group as in the series as a whole. On the other hand the degree of coronary sclerosis present in the 69 males and 52 females in the series with malignant neoplasms was significantly less than in the whole series. The hearts of 77 males and 39 females were hypertrophied owing to hypertension, and the degree of coronary sclerosis present in these cases was considerably greater than in the whole series, especially in the age range of 30 to 49 years, in which it was nearly the maximum degree measurable. The number of diabetics in the series was too small for reliable conclusions to be drawn. In the 36 subjects (30 male, 6 female) who died of coronary thrombosis or had had symptoms of coronary disease the degree of sclerosis was uniformly severe;

even in the youngest and least affected age group, 20 to 29, average grading for intimal infiltration was 10 points. In practically all cases in the series the site of greatest sclerosis was in the first 25% of the length of the vessels. In the majority of the hearts the degree of sclerosis was greater in the left than in the right coronary artery or equal in the two vessels, few showing more severe sclerosis in the right than the left coronary artery.

It is concluded from this investigation that the difference in the incidence of coronary sclerosis between males and females begins in early childhood before puberty and continues steadily up to and beyond the menopause, and that in both sexes coronary sclerosis is a continuous process throughout life. Since a severe degree of sclerosis is necessary before symptoms appear or death occurs, males are much more likely to attain this degree than females, and in consequence suffer a much higher mortality and morbidity from this cause. In view of the early age at which the sex difference is discernible it seems less likely to be due to hormonal influences than to an inborn basic difference of metabolism.

Peter Harvey

1496. **The Occurrence of Ceroid-containing Cells (" Fluorocytes ") in the Liver.** (Über das Vorkommen von ceroidhaltigen Zellen (" Fluorocyten ") in der Leber)
R. SCHMIDT. *Virchows Archiv für pathologische Anatomie und Physiologie und für klinische Medizin* [*Virchows Arch. path. Anat.*] **323**, 123–132, 1953. 6 figs., 21 refs.

The author, working at the Pathological Institute of the University of Marburg, has studied the occurrence of certain light-yellow, fluorescent cells, distinct from those containing lipofuscin or neutral fat, and called " fluorocytes " by Hamperl, in frozen and paraffin sections of material from 400 liver biopsies, the advantages of which over necropsy material for fluorescence microscopy are pointed out and briefly discussed. In their shape and situation these cells, which were present in at least one-quarter of the specimens, correspond to Kupffer cells. Whereas neutral-fat droplets are lost in the preparation of paraffin sections, the fluorescent material in these cells is retained and stains strikingly with Sudan III, while Turnbull blue sometimes gives it a slight blue hue. After digestion of their contained glycogen with diastase the cells stain well with Schiff's stain. From its staining reactions the author concludes that the pigment contained in these cells is identical with the " ceroid " of American authors. Since similar cells also occur in organs other than the liver, for example, in endometrial cysts, cervical polyps, and cystadenomata of the breast, they do not appear to be specifically connected with liver metabolism, and were thought by Hamperl to be " the expression of a peculiar digestion by macrophages of substances liberated during the breakdown of blood ".

In the author's series fluorocytes were found in 15% of normal livers, in almost 50% of cases of leukaemia, in 40% of cases of tuberculosis, and in 36 out of 40 cases of hepatitis at various stages of the disease. This, in the author's view, confirms the theory that ceroid is an indicator of cellular decomposition.

Ferdinand Hillman

1497. **The Lipofuscin of the Liver.** (Über das Lipofuscin der Leber)
K. D. BACHMANN. *Virchows Archiv für pathologische Anatomie und Physiologie und für klinische Medizin* [*Virchows Arch. path. Anat.*] **323**, 133–142, 1953. 7 figs., 14 refs.

The author investigated the occurrence of lipofuscin in 712 specimens of liver-biopsy material at the Pathological Institute of the University of Marburg. The exact arrangement of lipofuscin granules in the liver cells and the position of pigment-carrying cells in the acinus is described, and it is emphasized that lipofuscin must be distinguished from the larger, coarser, more easily stained, and strongly refractile lipid particles found in the peripheral part of the liver lobule.

A simple method of rough quantitative estimation of lipofuscin is described which was used to determine the average lipofuscin content of the liver in each 10-year age group of the author's series in order to test the time-honoured concept of lipofuscin as a " wear-and-tear " pigment. It was found that the proportion of cases with medium amounts of lipofuscin in the liver did in fact increase with advancing age, although the proportion of cases with large amounts of lipofuscin reached a peak in the 40–49 age group and declined afterwards. However, complete absence or a great excess of lipofuscin might occur at any age. Cachectic states, such as tuberculosis and neoplastic disease, were not associated with an increase in the lipofuscin content, while little or no lipofuscin was present in the liver in cases of hepatitis or cirrhosis in any age group. An inverse relationship could be demonstrated between the amounts of neutral fat and of lipofuscin present, and it was shown that lipofuscin present in the liver in large quantities may disappear entirely in the course of a few months. The author therefore rejects the " wear-and-tear " theory of origin of lipofuscin, and considers that its presence in the liver is usually due to metabolic disturbances before death.

Ferdinand Hillman

1498. **The Liver in Sickle Cell Anemia**
T. W. GREEN, C. L. CONLEY, and M. BERTHRONG. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **92**, 99–127, Feb., 1953. 16 figs., 16 refs.

The authors report the results of a study of liver function, over a number of years, in 50 patients with sickle-cell anaemia. About two-thirds of these patients showed clinical evidence of liver disease, which in a few cases was severe; the liver disorder seemed to be a specific manifestation of sickle-cell disease. In a histological examination of 21 cases coming to necropsy the liver changes suggested severe impairment of hepatic blood flow, due to the combined effects of anaemia, sickling of erythrocytes in the hepatic sinusoids, and obstruction by Kupffer cells engorged with phagocytosed blood cells. The latter two processes, which are unique to sickle-cell anaemia, were accompanied by morphological evidence of hepatic-cell injury. Definite cirrhosis of the liver was seen in 4 cases. The paper contains a very full account of the clinical and laboratory findings and some excellent photomicrographs.

Peter Story

1499. **The Morbid Histology of Viral Hepatitis.** (Zur Histologie der Virushepatitis)
H. THALER. *Schweizerische Zeitschrift für allgemeine Pathologie und Bakteriologie* [*Schweiz. Z. allg. Path. Bakt.*] **16**, 129–155, 1953. 15 figs., 40 refs.

The histological appearances of liver-biopsy material from 177 cases of viral hepatitis treated at the University Medical Clinic, Vienna, are reviewed. The histological changes, though not uniform, nevertheless formed a pattern which enabled some correlation with the progress and severity of the disease to be made. They showed that the chief damage is to the liver cell, which undergoes cloudy swelling, loses glycogen, and develops coarse eosinophilic granules. Later, more advanced degenerative changes take place, such as vesicular degeneration of the cytoplasm and pyknosis or abnormal mitosis of the nucleus. The changes are almost always centrilobular, but occasionally periportal cells are also affected. Hyaline eosinophilic bodies and cytoplasmic inclusion bodies were found early; these bodies are characteristic of viral hepatitis, though they bear no constant relationship to the progress of the disease. Even before the appearance of jaundice irregular focal reticulo-endothelial proliferation was seen, and later clumping of lymphocytes and plasma cells, and occasionally also of granulocytes, was noted. Proliferation of the bile ducts occurred as early as the second week of jaundice, but when this had subsided the only remaining histological change was often some irregularity of the liver lobules, particularly in their central portions. The development of fibrosis was not followed up in this study. In recurrent cases of hepatitis much the same histological picture was seen as in the primary attack. Similar changes have been observed in yellow fever.

[A review of the pathology of hepatitis, based on 136 liver-biopsy specimens obtained at the Postgraduate Medical School of London, was made by Weinbren (*J. Path. Bact.*, 1952, **64**, 395), whose findings were strikingly similar to those reported here from Vienna.]

E. Neumark

1500. **Effect of Isoniazid on Tuberculous Lesions of the Kidneys**
J. C. DICK. *Lancet* [*Lancet*] **1**, 808–817, April 25, 1953. 29 figs., 20 refs.

The effect of isoniazid on tuberculous lesions in the kidney was observed in 9 cases of renal tuberculosis at the Robroyston Hospital, Glasgow, the drug having been given for periods varying up to 3 months. Specimens were obtained at necropsy on one patient who died from uraemia and at nephrectomy in 8 patients, the operation having been indicated by cystitis in 7 and by deterioration of the general condition in one.

Three major changes were noted. (1) Caseous material was absorbed, the maximum effect being observed after one month's treatment. (2) The avascular zones of the lesions became vascularized; this could be recognized macroscopically as haemorrhages and congestion. (3) Epithelioid cell activity was considerably reduced. In addition, fibrosis did not develop and fibrous tissue already present became hyalinized and partially absorbed. In open lesions the maximum effect was observed after about one month's treatment, but in isolated lesions the effect was more satisfactory after a 3-month course.

Although relatively few specimens were examined the changes were uniform in many sections from the same patient. The lesions were also compared with those observed by the author in a much larger series of cases treated with streptomycin and PAS and in untreated cases.

J. B. Enticknap

1501. **Foetal Enteritis.** (Fetale Enteritis)
M. STAEMMLER. *Virchows Archiv für pathologische Anatomie und Physiologie und für klinische Medizin* [*Virchows Arch. path. Anat.*] **323**, 143–154, 1953. 6 figs., 19 refs.

In a previous communication (*Virchows Arch. path. Anat.*, 1951, **320**, 577) the author described a number of cases in which an attempt to procure abortion had led to infection of the amniotic fluid and of the respiratory and digestive tract of the foetus. He now reports his findings in a further case, in which there was strong circumstantial evidence of attempted criminal abortion and a male foetus of 25 cm. length was sent to him for examination at the Aachen Pathological Institute. Perforation of the small intestine had occurred and severe diffuse peritonitis was present, giving a pure culture of haemolytic streptococci. A large abscess was present in the umbilical cord, and the oesophagus contained clumps of streptococci and leucocytes. The intestinal mucosa showed extensive necrotizing enteritis which, in one circumscribed area, involved all the coats and had led to perforation. Reaction of the foetal tissue was very scanty and there was no suppuration, but only necrosis, near the perforation. The abscess in the umbilical cord is regarded by the author as an indication that the infection was primarily of the amniotic fluid.

The author then speculates on what would have happened if the foetus had been able to overcome the infection; a meconium peritonitis might have resulted, with obstruction of the intestinal lumen by kinks or adhesions following organization of the peritoneal exudate, or the lumen might have been obstructed by granulation tissue at the site of the perforation. It is therefore suggested that this type of case provides a basis for the inflammatory aetiology which has been postulated in some cases of congenital intestinal atresia.

Such a case is briefly reported, in which the lumen of the bowel was filled with scar tissue infiltrated with small lymphocytes, the picture resembling the appearance of an obliterated appendix.

In the second part of the paper 3 further cases of interstitial foetal enteritis of varying degree are reported. One of these foetuses, at the 30-cm. stage, showed distinct leucocytic response to the infection, whereas in the other foetuses, which were at an earlier stage of development, only a monocytic reaction was present. The infection in all three cases is assumed to have originated from an infected amnion. A varying degree of damage to the intestinal mucosa was present in all cases and was attributed to direct action of the bacteria.

Ferdinand Hillman

Bacteriology

1502. **Augmentation Influence of Influenza Virus on Associated Infections.** (Influence favorisante du virus grippal sur les infections associées)
P. BORDET and L. QUERSIN-THIRY. *Annales de l'Institut Pasteur* [*Ann. Inst. Pasteur*] **84**, 695–702, April, 1953. 4 refs.

The authors had previously demonstrated the increased toxicity of *Haemophilus influenzae* in guinea-pigs which had been injected earlier with influenza virus, and had also found that organisms grown in solid media gave better results than those grown in broth: they therefore used solid media for all experiments in this series carried out at the Institut Pasteur, Brussels. Guinea-pigs were inoculated with *H. influenzae* injected into the peritoneal cavity, one group of animals having received an injection of influenza virus half an hour earlier by the same route. The fatal dose of *H. influenzae* for the animals previously inoculated with virus was about 1/250 of the fatal dose for the control animals.

Similar experiments were performed with other organisms. With *Bacterium coli* the lethal dose was the same in both groups of animals. With *Diplococcus pneumoniae* the lethal dose in the virus-infected animals was 1/10, and with a haemolytic streptococcus 1/100 to 1/200, of the lethal dose in the control group. The authors suggest that this effect is not cumulative, but is due to the previous sensitization by the virus, and point out that the effect is greatest with those organisms which are the usual secondary invaders in influenza. They also show that this toxic effect of the influenza virus is independent of the haemagglutination power, the toxic fraction being more heat-labile than the haemagglutination fraction, nor is the toxic action affected by mixing with egg albumen or by adsorption on aluminium hydroxide. *R. F. Jennison*

SEROLOGY AND IMMUNOLOGY

1503. **Group A Polysaccharide Precipitin Reactions in Acute Streptococcosis and Rheumatic Fever**
L. WEINSTEIN. *Yale Journal of Biology and Medicine* [*Yale J. Biol. Med.*] **25**, 349–357, April, 1953. 11 refs.

After a review of previous work on the significance of the presence in the serum of antibodies to group specific streptococcal polysaccharides in the rheumatic diseases, the author details his own findings at the Massachusetts Memorial Hospitals (Boston University School of Medicine) in sera from 151 patients with streptococcal infections, 76 patients with acute rheumatic fever, and 310 patients with other diseases. The precipitating antibody for purified Group-A carbohydrate was detected by layering the bacterial extract over the serum and incubating at 37° C. for 2 hours and then transferring to a refrigerator. Readings were made at 24 hours, 48 hours, and 72 hours, control tubes being set up containing bacterial extract and saline or serum and saline. (The details of preparation of the bacterial extract containing group specific polysaccharide are given in full.) Serum was obtained from each patient at the time of admission and again 14 days later. A positive precipitin reaction was obtained in 34% of the group with streptococcal infections (without non-suppurative complications), in 24% of the group with acute rheumatic fever, and in proportions ranging from 0 to 100% in the various other diseases. These results are somewhat at variance with other published results, possibly owing to the author's method of purification of the extract, which is simpler than that usually employed but is claimed to be more efficient. The extract was free from type specific nucleoprotein, since there was no precipitation with potent Type-3 specific antiserum.

The author concludes that antibody may frequently be present in a patient's serum without other evidence of streptococcal infection, that its absence does not exclude the presence of streptococcal infection or rheumatic fever, and that hypersensitization to Group-A specific polysaccharide is of no significance in the pathogenesis of the rheumatic state. *E. G. L. Bywaters*

1504. **The Influence of ACTH and Cortisone on Experimental Antibody Production in Rabbits**
S. MOESCHLIN, R. BÁGUENA, and J. BÁGUENA. *International Archives of Allergy and Applied Immunology* [*Int. Arch. Allergy*] **4**, 83–100, 1953. 2 figs., 18 rfs.

A number of workers in recent years have been concerned with the influence of ACTH (corticotrophin) and cortisone on antibody production in experimental animals. The present authors, continuing their studies on plasma-cell development during antibody formation, now describe the results of their investigation, carried out at the University of Zürich, of the influence of ACTH and cortisone on these responses in the rabbit. Previously, they had shown that antibody formation could be related to plasma-cell response in the spleen of rabbits and, in common with other workers, that administration of ACTH and cortisone could depress the formation of antibody in rabbits undergoing immunization against certain antigens. The present experiments were planned to obtain more detailed information about the effect of these substances on the antibody and plasma-cell response of rabbits, the immunizing agent used being a polyvalent typhoid–paratyphoid vaccine. [This was presumably of the heat-killed phenol-preserved type, since the antibody response was measured by the paratyphoid BH serum agglutinin titre. Precise details of the agglutination technique are not given, nor do the authors state whether the agglutinable suspension used for the test was a standardized monophasic suspension or a simple diphasic killed broth culture.]

The animals were first sensitized with an injection of the polyvalent vaccine, and after irregular intervals (generally about 3 weeks) they were re-injected with the vaccine, given intravenously. The treated animals received either cortisone or ACTH for varying periods and at different intervals in relation to the re-injected vaccine in the several series of experiments. Blood tests were made before re-injection, and finally the animals were bled out at different stated intervals, killed, and plasma-cell counts carried out on spleen smears; the same procedure was followed in the control animals, and the agglutinin response and plasma-cell counts were compared in the two groups.

In general, the authors showed that ACTH or cortisone, given either 2 hours or 10 minutes before, or simultaneously with, the intravenous re-injection of the vaccine, had little or no effect on the antibody or plasma-cell response. When, however, the hormones were given 7 days before the re-injection of the vaccine, there was a marked decrease in antibody production, and also a reduction in the absolute number of plasma cells in the spleen. [These findings are shown in two series of graphs, but it is difficult to follow the detailed results as given in various tables.] *H. J. Bensted*

1505. **Preliminary Trials of Living Rabbit-fixed Virus in the Prophylaxis of Poliomyelitis. The Innocuity of the Method.** (Premiers essais de prophylaxie de la poliomyélite par virus vivant fixé au lapin. Innocuité de la méthode)

G. BLANC and L. A. MARTIN. *Bulletin de l'Académie nationale de médecine* [*Bull. Acad. nat. Méd.* (*Paris*)] **137**, 230–234, April 21, 1953. 2 figs.

The authors have previously shown (*Bull. Acad. nat. Méd.* (*Paris*), 1952, **136**, 655; *Abstracts of World Medicine*, 1953, **14**, 9) that rabbit-fixed poliomyelitis virus is harmless to man, and that when given orally it persists in the stools for a long time. They now bring further evidence of its innocuity when used on a large scale as a prophylactic.

The method of preparation of the vaccine is as follows. The organs (blood, liver, spleen, brain, and spinal cord) of virus-infected rabbits are finely ground and emulsified in 5 times their own weight of glycerin; the emulsion is then diluted with an equal part of a buffer solution, filtered through gauze, and penicillin and streptomycin added. This emulsion keeps for 2 months at −20° to −30° C. Before use, tests for bacterial sterility and for virulence to rabbits are carried out. The oral dose is 10 ml.—the equivalent of 1 g. of rabbit organs.

Following the occurrence of 5 cases of poliomyelitis in a thickly populated quarter of Casablanca "Old Town", 4,774 children between the ages of 3 weeks and 15 years, constituting the great majority of those living in the immediate vicinity, were given this emulsion, while in a suburban slum where 2 cases of poliomyelitis had occurred, another 925 child contacts were also treated. The emulsion was well tolerated, and no reaction of any kind was observed. No case of poliomyelitis developed among those treated or among the population of the adjoining areas The authors conclude that the rabbit-fixed virus is quite innocuous to man, but advance no claim as to its prophylactic value. This they suggest should be tested in regions where the disease is endemic or recurs periodically.

[It is now 3 years since these workers first reported that poliomyelitis virus (Brünhilde and Lansing types) could be readily adapted to the rabbit. So far their findings do not appear to have been confirmed, and no crucial experiments on monkeys to determine the protective value of the modified virus have been carried out.] *L. J. M. Laurent*

1506. **Immunization against Diphtheria. The Booster Dose**

J. H. MASON, M. ROBINSON, and M. S. BROWN. *South African Medical Journal* [*S. Afr. med. J.*] **27**, 293–295, April 11, 1953. 13 refs.

It was the practice in the City Health Department, Johannesburg, to give probationer nurses 0·5 Lf of unadsorbed diphtheria toxoid-antitoxin floccules (D.F.) intracutaneously at the same time as the preliminary Schick and Schick control tests were carried out, the object being to determine the sensitivity of individuals to D.F. Nurses giving a pseudo-Schick reaction and/or a reaction at the D.F. site did not receive a booster dose of D.F., but when a sample of blood, taken 14 days later, was assayed for antitoxin adequate amounts of circulating antibody were found. It was suspected from this that the small dose of 0·5 Lf of D.F. had acted as a booster dose, causing comparatively little inconvenience.

Tests were carried out to determine the serum antitoxin level before, and 14 to 21 days after, an intracutaneous dose of 0·5 Lf of D.F. in 104 Schick-negative persons, half of whom had a history of immunization dating back 1 to 14 years. The increase in circulating antibody in those with initial low levels (0·004 to 0·04 unit per ml.) was striking. Of 49 such people, 47 developed titres of more than 0·1 unit per ml. and 44 titres of 0·5 unit per ml. or more. In those with an original titre of more than 0·5 unit per ml. the relative increase in circulating antitoxin was not so great, a result attributed to the "swamping" effect of the circulating antibody on the small amount of antigen injected. In 9 Schick-positive subjects no rise in antitoxin was detected, and these, the authors consider, were probably "poor responders" to immunization.

The authors recommend that in the selection of adults for diphtheria immunization, 3 intracutaneous injections should be given simultaneously: the Schick and Schick-control sera and a dose of 0·5 Lf of the particular antigen to be administered. In Schick-positive subjects who do not react at the antigen site a full course of immunization can be started. In Schick-negative subjects and in those with a pseudo-reaction and/or a reaction at the antigen site no further injections are necessary. *K. S. Zinnemann*

1507. **Antityphoid Immunization by the Percutaneous Route.** (Immunizzazione antitifica per via percutanea)

A. CANDELI and M. ANGORI. *Annali d'igiene* [*Ann. Igiene*] **4**, 261–264, July–Aug., 1953. 4 refs.

Pharmacology

1508. **The Effect of Histamine and Antihistamines on Body Temperature**
E. W. PACKMAN, G. V. ROSSI, and J. W. E. HARRISSON. *Journal of Pharmacy and Pharmacology* [*J. Pharm. Pharmacol.*] **5**, 301–310, May, 1953. 10 figs., 22 refs.

Both histamine and antihistamines cause a decrease in the body temperature of mice, rats, and guinea-pigs. Neither of these agents has any effect on the body temperature of rabbits. Antihistamines reduce the body temperature of normal animals as well as of those with artificially induced fever, therefore this effect cannot be attributed to a true antipyretic activity. The body temperature decreasing action of histamine as well as of antihistamines is greater at lower environmental temperatures. There is no parallelism between the body temperature decreasing effect of the 15 antihistamines tested and their antihistaminic potency, antianaphylactic activity, atropine-like effect, hypnotic action, and acute toxicity. The possible mode of action of histamine and antihistamines on body temperature has been discussed. —[Authors' summary.]

1509. **Pharmacology of Vinyl Ethynyl Carbinols—a New Class of Central Nervous System Depressants**
S. Y. P'AN, J. F. GARDOCKI, M. HARFENIST, and A. BAVLEY. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **107**, 459–463, April, 1953. 7 refs.

Vinyl ethynyl carbinols are substituted straight-chain molecules of five carbon atoms and take the form of mobile, colourless liquids with a pleasant odour. According to the authors, who carried out experiments with these compounds on animals, they are effective against leptazol-induced convulsions in mice when given orally or by injection. They exert a hypnotic action on the central nervous system, and administration for 14 days in large doses had no apparent harmful effects on rats or dogs. Their potency was found to be less than that of phenytoin. *James D. P. Graham*

1510. **The Pharmacology of N-Benzyl-β-chloropropionamide (Hibicon), a New Anticonvulsant**
B. K. HARNED, R. W. CUNNINGHAM, M. C. CLARK, C. H. HINE, M. M. KANE, F. H. SMITH, R. E. VESSEY, N. N. YUDA, and F. W. ZABRANSKY. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **107**, 403–423, April, 1953. 2 figs., 24 refs.

"Hibicon" (N-benzyl-β-chloropropionamide), a new anticonvulsant said to possess a similar degree of potency and effectiveness to phenytoin, is a white crystalline solid, soluble in water up to 1·3% at 100° C. It was found to be less active than phenytoin when the two compounds were compared by means of the maximal electro-shock seizure test in rats (a measure of general anticonvulsant activity). The Putnam–Merritt test in cats (which differentiates between drugs active against grand mal and against petit mal) showed that hibicon belongs to the same pharmacodynamic group as phenobarbitone and phenytoin. It was also found to protect against leptazol given intravenously and was of a similar potency to phenytoin when tested on mice. In rats oral hibicon exerted its maximum anticonvulsant effect in 2 hours, and a detectable effect remained for 12 hours. Unilateral nephrectomy or administration of carbon tetrachloride delays the action of hibicon, indicating that the latter is partly detoxified in the liver and partly excreted in the urine. In acute overdosage a condition resembling decerebrate rigidity is caused in animals, but no evidence of chronic toxicity was observed in rats and dogs given large amounts daily for a year or more.

[It would seem that this compound might be an effective, non-toxic, and specific anticonvulsant with the same clinical range of effectiveness as phenytoin. It may therefore be of value as a substitute for that drug in patients who are intolerant to it.]
James D. P. Graham

1511. **The Use of Levo-dromoran Tartrate (Levorphan Tartrate) for Relief of Postoperative Pain**
R. D. HUNT and F. F. FOLDES. *New England Journal of Medicine* [*New Engl. J. Med.*] **248**, 803–805, May 7, 1953. 14 refs.

A description is given of a clinical trial undertaken in the Department of Anesthesiology of Pittsburgh University to compare the effectiveness of the laevorotatory isomer of "dromoran" (methorphinan) with that of the racemic form in the relief of pain following operation. It had previously been shown from both animal experiments and observations on man that the dextrorotatory isomer had no analgesic activity. In the present study 1,067 subcutaneous injections of "levorphan tartrate" (the laevorotatory isomer) were given to 311 patients. The method of selecting patients and that of conducting the trial were the same as those used in a previous investigation (*New Engl. J. Med.*, 1951, **244**, 286), in which the effect of racemic dromoran on 311 postoperative patients was compared with that of 10 mg. of morphine sulphate on 312 patients, so that it was possible to correlate the results of both trials.

The relief of pain was recorded as "complete" when the patient had no pain for 3 hours or more after injection, lesser degrees of relief being described as "moderate", "slight", or "none". On this basis the first postoperative dose of levorphan afforded complete relief in 77·2% of patients, while the figures (obtained from the previous trial) for comparable doses of dromoran and morphine were 66·5 and 46·2% respectively. There was no relief from pain in 1% of the patients given levorphan, 2·6% of those given racemic

dromoran, and 5·8% of those receiving morphine. Subsequent doses of both the laevorotatory and racemic forms of the drug gave complete relief in a greater percentage of cases than was obtained with morphine. The total incidence of side-effects with all three drugs was approximately equal. The frequency of diaphoresis was lower with levorphan tartrate than with morphine, whereas the opposite was true of racemic dromoran. Dryness of the mouth, drowsiness, and " grogginess " were more commonly observed with levorphan and with racemic dromoran than with morphine.

It was observed that a dose of levorphan had greater analgesic effect than the quantity of racemic drug containing the same dose—which might be explained by the dextro-isomer having an inhibitory effect on levorphan analgesia—and that the incidence of side-effects of the two forms was approximately the same.

Robert Hodgkinson

1512. **Clinical Experiences in the Use of N-Allylnormorphine (Nalline) as an Antagonist to Morphine and Other Narcotics in Surgical Patients**
J. ADRIANI and M. KERR. *Surgery* [*Surgery*] **33**, 731–736, May, 1953. 6 refs.

N-Allylnormorphine (" nalline "), which consists structurally of a morphine molecule in which the methyl group on the nitrogen atom is replaced by an allyl group, was used as an antagonist to morphine in 48 surgical cases at the Charity Hospital, New Orleans. The solution is colourless, and is unstable in air or in rubber-capped bottles but stable in sealed ampoules. The strength of the solution used was 5 mg. in 1 ml. In doses of 2·5 to 20 mg. intravenously it relieved the respiratory depression caused by narcotics of the morphine group and by pharmacologically similar drugs such as pethidine, the relief being sustained. It was ineffective in respiratory depression caused by barbiturates and did not overcome respiratory difficulties due to anoxia. A slight, transient rise in blood pressure was observed in some patients when doses up to 20 mg. were given; with large doses (30 to 40 mg.) there was a fall in blood pressure. The authors state that the drug did not cause convulsions; [no other side-effects are reported].

Nine of the 48 cases are described in detail.

E. K. Brownrigg

1513. **Mode of Action of Tromexan**
R. B. HUNTER and G. R. TUDHOPE. *Lancet* [*Lancet*] **1**, 821–823, April 25, 1953. 1 fig., 21 refs.

In this investigation, carried out in the Department of Pharmacology, St. Andrews University Medical School, of the effect of " tromexan " (ethyl biscoumacetate) on prothrombin activity, the clotting time of plasma from a patient who had received tromexan was compared with that of normal control subjects, with and without the addition of the unstable prothrombin accelerator, Factor V, or of the stable accelerator known as Factor VII. It was found that the clotting time was not modified by the presence or absence of added Factor V, but was markedly decreased by the addition of Factor VII. It follows that tromexan acts, like dicoumarol, by decreasing the amount of Factor VII normally present. A comparison of the methods of Quick and of Owren for the determination of prothrombin indicated that Owren's method is not markedly superior to the rather simpler method of Quick. It was confirmed that commercial " thromboplastin " preparations from animal brain used up to now are deficient in both Factor V and Factor VII, and recent views on thromboplastin generation are discussed.

V. J. Woolley

1514. **An Experimental Study of the Anticoagulant " Marcoumar " (3-(1′-Phenyl-propyl)-4-oxycoumarin) and its Antagonist " Konakion " (Synthetic Vitamin K_1).** (Experimentelle Untersuchungen über das Antikoagulans Marcoumar (3-(1′-Phenyl-propyl)-4-oxy-cumarin) und seinen Antagonisten Konakion (synthetisches Vitamin K_1)
R. JÜRGENS. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **83**, 471–475, May 16, 1953. 8 figs., 31 refs.

The results of experiments carried out on animals to study the action of a number of analogues of dicoumarol are reported, and the physical and chemical details of a new anticoagulant, " marcoumar ", are presented. From estimations of the prothrombin time after giving single and multiple doses orally, rectally, or intravenously to small animals, it was shown that this drug has a more protracted action than any of the other anticoagulants at present available. Acute and chronic toxicity studies showed it to be relatively safe. Its effect was found to vary with the species of laboratory animal used, being greatest in dogs and smallest in rabbits. " Konakion ", a synthetic vitamin-K_1 analogue, was found to be a reliable and rapid antagonist against marcoumar and all other dicoumarol analogues examined.

Robert Hodgkinson

1515. **A New Highly Active Anticoagulant with Prolonged Effect (" Marcoumar ").** (Über ein neues, hochaktives Antikoagulans mit protrahierter Wirkung (Marcoumar)
F. KOLLER and H. JAKOB. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **83**, 476–479, May 16, 1953. 5 figs., 16 refs.

There is a need for an anticoagulant with a constant and predictable effect on the prothrombin time. Such an attribute is closely related to the duration of activity of the preparation, since a short-acting drug produces marked fluctuations in the prothrombin time. Short-acting coagulants have, however, been used in preference to longer-acting ones in the past since, in the absence of an effective antidote, they were safer as their action was more short-lived. Now that the prothrombin time can be rapidly raised by the administration of vitamin K_1, there is no reason why a long-acting anticoagulant should not be used.

The action of marcoumar [see Abstract 1514] was investigated at the University Medical Clinic, Zürich, on 40 patients suffering from thrombosis, 33 suffering from myocardial infarction, 20 suffering from pulmonary infarction, and 7 with miscellaneous diseases. The average dose required was 20 mg. on the first day, 10 mg.

on the second day, and an average maintenance dose of 3 mg. daily. It was therefore effective in one-tenth to one-hundredth of the dosage of other anticoagulants. On this dose the prothrombin time was kept within the therapeutic optimum limits for about 14 days.

Robert Hodgkinson

1516. **Preliminary Evaluation of a New Drug, Antrenyl. Effect on Gastric Secretion, Motility and Results in the Symptomatic Care of Peptic Ulcer**

P. E. MATTMAN and L. STRUTNER. *American Journal of Digestive Diseases* [*Amer. J. dig. Dis.*] **20**, 126–135, May, 1953. 5 figs., 28 refs.

A new anticholinergic drug, " antrenyl "—diethyl(2-hydroxyethyl)methylammonium bromide α-phenyl-*cyclo*-hexaneglycolate—was given a clinical trial at the Detroit Receiving Hospital and the Dearborn Veterans' Administration Hospital, Detroit, Michigan, in the treatment of simple peptic ulcer.

In the first part of the investigation the effect of the drug, given intramuscularly or by mouth, on the volume and on the free and combined acidity of the gastric secretion was compared with those of placebos and of atropine. Specimens were collected at 15-minute intervals for 4 hours through a Levine tube connected to a continuous-suction machine operated at a negative pressure of 120 mm. Hg. In 3 cases 2 mg. of antrenyl given intramuscularly caused a marked fall in the volume, as compared with a rise after the injection of 1 ml. of normal saline. The level of free acid fell after the administration of antrenyl, while after saline had been given there was a fall in 2 cases and a rise in one. The combined-acid level showed no consistent change. In 5 cases the effects of intramuscular injection of 0·5 to 2·0 mg. of antrenyl were similar to those produced by 0·43 to 0·87 mg. of atropine, both as regards the gastric secretion and in their side-effects, consisting in blurring of vision and dryness of the mouth. In 5 cases 50 mg. of antrenyl was introduced directly into the stomach, night specimens of gastric juice being obtained at half-hourly intervals for 3 hours. As compared with placebos, which produced variable effects, antrenyl in this dosage, which was considered too high for regular use, caused consistent and appreciable falls in the total volume and in the level of free acid, while there were no consistent changes in the combined-acid level. Similar results were obtained in a further 5 cases without controls. In 3 cases the effects of intragastric administration of 30 mg. of antrenyl were similarly observed. The volume of gastric secretion fell markedly, but the changes in acidity were variable.

In the second part of the investigation, which was devoted to studies of gastric motility, 5 patients were given, on separate days, 50 mg. of antrenyl and a placebo, in each case followed in half an hour by 100 mg. of barium sulphate in 6 oz. (170 ml.) of water. The patient was radiographed half an hour later and then at hourly intervals, the proportion of barium remaining in the stomach and the time taken for the head of the column to reach the ileo-caecal junction being noted. Antrenyl caused a marked slowing of gastro-intestinal activity, up to 50% of barium being retained in the stomach for 3 hours, while the ileo-caecal valve was in some cases not reached within 9 hours. In the control experiment the stomach was always empty after 3 hours, by which time the barium had reached the terminal ileum. In one case 100 mg. of antrenyl caused a virtual stoppage of gastro-intestinal activity. All patients complained of side-effects.

In the third part of the study the effect on symptoms of antrenyl in doses of 25 mg. 6-hourly was compared with that of 1·3 ml. of a belladonna mixture. Two groups of 11 patients each were treated, the patients being comparable in respect of age, previous hospital treatment, duration of symptoms, and radiological findings, although at the time of the trial radiologically demonstrated ulcers predominated in the belladonna-treated group, whereas there was a preponderance of duodenal lesions in the group given antrenyl. Both groups showed improvement as regards pain generally, night pain, and epigastric tenderness, the improvement being more rapid in the antrenyl-treated patients. Toxic effects also were more marked in the group receiving antrenyl. Night specimens of gastric secretion were obtained in both groups after 10 to 14 days of therapy. There was no significant change in acidity, free or combined, in either group, but the antrenyl-treated group showed a fall of 50% in the volume of secretion.

H. F. Reichenfeld

1517. **Studies on a New Anticholinergic Drug, Antrenyl**

B. R. ROWEN, W. H. BACHRACH, J. A. HALSTED, and H. SCHAPIRO. *Gastroenterology* [*Gastroenterology*] **24**, 86–102, May, 1953. 3 figs., 6 refs.

In this paper are described experimental and clinical trials at the Wadsworth General Hospital and University of Southern California, Los Angeles, of the new anticholinergic drug, " antrenyl " [see Abstract 1516]. Its effect on alimentary motility was investigated by the multi-balloon technique. It was found to inhibit all intestinal movement, both spontaneous in origin and that induced by morphine or cholinergic drugs. The most rapid and consistent results were obtained by intravenous administration in doses of 3 mg.; the drug was also effective when given by mouth in doses of 5, 10, and 25 mg. Gastric analysis revealed some diminution of total gastric secretion with a corresponding fall in acid production. No significant effect on gastric secretion was, however, produced when doses too small to produce side-effects were given. Patients suffering from duodenal ulcer were more resistant to its inhibitory action than were healthy control subjects. When given therapeutically to patients with peptic ulcer, antrenyl proved a satisfactory substitute for atropine. In a large series of patients it had no toxic effects other than those due to its anticholinergic qualities.

The authors consider antrenyl a satisfactory drug for use in conjunction with other standard therapeutic measures in the treatment of duodenal ulcer. They present no evidence, and are themselves not convinced, that it has any advantages over atropine.

A. G. Parks

Chemotherapy

1518. **The Mode of Action of Isoniazid.** (Iets over de werking van *iso*-nicotinezuur-hydrazide (I.N.H.))
H. L. WOLFF. *Nederlandsch tijdschrift voor geneeskunde* [*Ned. T. Geneesk.*] **97**, 1262–1265, May 16, 1953.

Observations made at the University of Leiden in the course of investigations into the sensitivity of tubercle bacilli to isoniazid are reported. Growth occurred on solid media in the presence of a higher concentration of isoniazid than in fluid media, and when the concentration did not inhibit growth, growth occurred earlier than in control tubes without isoniazid. This growth-stimulating effect is compared with that of streptomycin and is regarded as more strictly an acceleration of growth; it occurs over a wider concentration range than is the case with streptomycin. The growth-stimulating properties are not a direct function of concentration and are seen only with those strains against which isoniazid in higher concentration is bacteriostatic rather than bactericidal. Attempts to apply this phenomenon for the earlier isolation of the bacilli did not yield definitely satisfactory results; although results were obtained earlier, the saving in time did not appear sufficient to compensate for the technical difficulties involved.

R. Crawford

1519. **Mode of Action of Isoniazid**
W. R. BARCLAY, R. H. EBERT, and D. KOCH-WESER. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **67**, 490–496, April, 1953. 3 figs., 11 refs.

Isoniazid, a simple chemical compound, is specifically bacteriostatic against mycobacteria at concentrations as low as 0·02 μg. per ml. of medium. The authors, working at the University of Chicago, have attempted to clarify its mode of action by quantitative growth studies and by determining the uptake of the drug when labelled with radioactive carbon in the carboxyl group. In the growth studies Dubos's 23 "tween"–albumin liquid medium and a virulent strain of *Mycobacterium tuberculosis* (H37Rv) were used. Strains resistant to 60 μg. of isoniazid per ml. were obtained, but those resistant to 20 μg. per ml. were used as they grew as quickly as their parent stock. Growth curves were obtained by measurement of turbidity, being the percentage transmission converted to mg. of organisms (wet weight) per ml. by using a previously calibrated scale.

It was found on adding isoniazid or streptomycin after either 5 or 9 days' growth that isoniazid did not cause an immediate cessation of growth. This sulphonamide-like effect was the same for both large and small numbers of organisms and was independent of drug concentration (0·05 to 100 μg. per ml.). With lower concentrations of the drug cell multiplication began again after some 2 weeks, and these new cells were resistant to isoniazid. In contrast, streptomycin caused an almost immediate cessation of growth, with decreased turbidity in 3 days reflecting a bactericidal action also shown by absence of tetrazolium reduction. Resistant strains gradually appeared, however, and growth began again. A small amount of antibiotic (1 μg. per ml.) added on the 9th day produced a decline, but no arrest, in growth rate.

Study of the uptake of radioactive isoniazid by susceptible and resistant strains of *Myco. tuberculosis* in either Proskauer and Beck's or Dubos's medium showed that the sensitive organisms took up from 30 to 200 times as much as the resistant strains. The authors suggest that the action of isoniazid is initially bacteriostatic rather than bactericidal, and that it produces bacteriostasis by interfering with the formation of a metabolite essential to growth. The possible constitution and function of this metabolite are discussed.

Malcolm Woodbine

1520. **Synergistic Effect of Sulfadiazine and Daraprim Against Experimental Toxoplasmosis in the Mouse**
D. E. EYLES and N. COLEMAN. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **3**, 483–490, May, 1953. 3 figs., 4 refs.

"Daraprim" (pyrimethamine), 2 : 4-diamino-5-*p*-chlorophenyl-6-ethylpyrimidine, is an antagonist to folic acid. Previous work at the U.S. National Institutes of Health Laboratory of Tropical Diseases having shown that it was active against toxoplasmosis in mice, the present study was undertaken to determine if there was a synergistic effect with sulphadiazine (which is an antagonist to *p*-aminobenzoic acid), as had been shown to occur with sulphadiazine in combination with a closely related drug of the pyrimidine group against the malaria organism *Plasmodium gallinaceum*.

Mice were infected with *Toxoplasma gondii* and the drugs were given in the diet. The median effective dose of each of the drugs given by itself was 40 mg. % [*sic*] for sulphadiazine and 9 mg. % for daraprim; but the most effective combination of the two was 5 mg. % of sulphadiazine with 0·37 mg. % of daraprim. It is thus clear that there is a marked synergistic effect between the two compounds. Moreover the proportion of mice completely cured was much greater with this combination than with maximum tolerated doses of either drug by itself. But increasing the dose of the combined drugs did not increase the rate of cure, which was never more than 78% of the animals. The greater the dose of *Toxoplasma* inoculated, the greater the mortality, in spite of treatment. Treatment was effective even if delayed as long as 4 days after inoculation, but after this its effect was greatly diminished.

When daraprim was combined with "diasone" (a sulphone compound, sulfoxone sodium) there was some synergistic effect. Proguanil alone had no effect, but when combined with sulphadiazine it had a slight

potentiating effect. From the clinical standpoint, these results suggest that a combination of daraprim and sulphadiazine might have a valuable therapeutic effect in human infections, although caution will be needed at first. From the scientific point of view, they indicate that both drugs act on the same metabolic pathways, presumably those involving *p*-aminobenzoic acid and folic acid. [It seems probable that *p*-aminobenzoic acid (and possibly also folic acid) is a growth factor for *Toxoplasma*.] *F. Hawking*

See also Tuberculosis, Abstract 1546.

ANTIBIOTICS

1521. **Cross-resistance in Staphylococci and the Effect of Combinations of Antibiotics on Resistant Strains**
B. T. MIYAHARA, K. CARIKER, and W. E. CLAPPER. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **41**, 550–558, April, 1953. 26 refs.

A high percentage of penicillin-resistant coagulase-positive and coagulase-negative strains of staphylococci were found in cultures from patients in Colorado General Hospital. Resistance to aureomycin, chloramphenicol, streptomycin, and terramycin was almost always accompanied by resistance to penicillin; and cross-resistance was seen between terramycin and aureomycin, but much less between these antibiotics and chloramphenicol. More strains were sensitive to chloramphenicol than to any other antibiotic.

Each of seven strains of penicillin-resistant, and one penicillin-sensitive staphylococcus differed in its susceptibility to combinations of aureomycin, bacitracin, chloramphenicol, penicillin, streptomycin, and terramycin. This indicates that each strain must be tested to determine the most effective combination for preventing growth. The combination of penicillin and streptomycin acted additively or synergistically against more strains than any other combination. The only combination to show antagonism was streptomycin and chloramphenicol, and this was shown with only one strain. Streptomycin was one of a synergistic pair more often, and chloramphenicol less often, than any of the other antibiotics. Synergistic combinations were found more often with the highly resistant strains, but the concentrations required to inhibit growth were still often very high.—[Authors' summary.]

1522. **The Inactivation of Antibiotics by Cation Exchange Resins**
I. S. FRIEDMAN, S. ZUCKERMAN, and E. MCCATTY. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **225**, 399–401, April, 1953. 4 refs.

With the increasing use of cation-exchange resins in the treatment of oedema states, the problem arises as to whether these resins will inactivate drugs orally and concurrently administered. The authors, working at the Jewish Sanitarium and Hospital for Chronic Diseases, New York, have determined by means of a filter-paper-strip technique the effect, if any, of the resins on the inhibition of growth of *Micrococcus citreus*, *Bacterium coli*, a streptococcus, and a paracolon bacillus by four commonly used antibiotics. Standard solutions of penicillin (50 units per ml.), chloramphenicol (250 μg. per ml.), dihydrostreptomycin (500 μg. per ml.), oxytetracycline ("terramycin") (200 μg. per ml.), and aureomycin (100 μg. per ml.) were used, and the filter-paper strips were immersed, drained, and centred on blood agar plates containing the organisms. The standard solutions were then shaken or allowed to stand in contact with the resin (in a concentration of 2 g. per 20 ml.) and the filter-paper-strip procedure repeated.

It was shown that resin alone did not inhibit growth or affect the degree of inhibition (by zone measurement) by either penicillin or chloramphenicol, that dihydrostreptomycin immediately lost its activity, and that oxytetracycline and aureomycin were inactivated by contact for less than 5 hours. *Malcolm Woodbine*

1523. **The Effect of Aureomycin and Chloramphenicol on the Fungal and Bacterial Flora of Children**
J. J. MCGOVERN, R. H. PARROTT, C. W. EMMONS, S. ROSS, F. G. BURKE, and E. C. RICE. *New England Journal of Medicine* [*New Engl. J. Med.*] **248**, 397–403, March 5, 1953. 1 fig., 24 refs.

An investigation was carried out at the Children's Hospital and National Institutes of Health, Washington, D.C., into the effect of certain antibiotics on the bacterial flora of the gastro-intestinal tract in children. In the first part of the study examination of cultures from 100 normal children revealed *Candida albicans* in the mouth in 14 cases; this organism was also found in 4 of the 68 stools examined. In the second part, aureomycin and chloramphenicol were given to selected groups of children and cultures from the mouth and rectum examined.

Aureomycin was given by mouth to 21 children in a dose of 40 to 50 mg. per kg. body weight per day for 8 days. *C. albicans* was cultured from the gastro-intestinal tract (mouth or rectum, or both) in 5 of the subjects before treatment and in 6 after the course was completed. Other species of organism appeared after treatment for the first time in 4 cases. In the mouth, streptococci and *Neisseria catarrhalis* were reduced in numbers; in the rectum, there was some reduction in the number of *Bacterium coli*, but the effect on *Pseudomonas aeruginosa* and *Proteus vulgaris* was less striking. Bacterial flora became normal 3 to 5 days after administration of the drug ceased, whereas it took 6 to 12 days for the fungal flora to become normal again. There was no clear correlation between gastro-intestinal complications and the high incidence of *C. albicans*.

Chloramphenicol was given by mouth to 15 children in a dose of 100 mg. per kg. body weight per day for 14 days. *C. albicans* was isolated before treatment from the mouth in 2 and from the rectum in one; the figures after treatment were 4 and 3 respectively. The organism was not isolated from the vagina. Other species of *Candida* were isolated before treatment from the mouth in one subject and from the rectum in 2; after treatment they were isolated from the mouth in 4 subjects and from the rectum in 6. They were also found in the vagina of

3 children after treatment, although none was found before chloramphenicol was given. Organisms appeared after treatment for the first time at 72 hours.

Chloramphenicol was given by intramuscular injection to 9 children. A few colonies of *C. albicans* were grown from the mouth of one patient before the drug was given, but by the eighth day of treatment a heavy growth was obtained from 4. The fungal flora began to decrease within 3 days of cessation of the drug and was normal, as a rule, by the end of 14 days. No undesirable gastro-intestinal symptoms could be attributed to the presence of large numbers of *C. albicans* in the mouth or rectum.

A. W. H. Foxell

1524. **Antagonism and Addition from Combinations of Aureomycin and Penicillin in the Treatment of Pneumococcic Infections in Mice**

G. G. JACKSON, M. H. LEPPER, J. SETO, and H. F. DOWLING. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **225**, 525–534, May, 1953. 4 figs., 12 refs.

As the number of antibiotics increases, greater interest is taken in the combination of two or more of these drugs in treating recalcitrant infections. The authors, at the University of Illinois College of Medicine, Chicago, have studied the treatment of pneumococcal infections in mice to determine whether addition or antagonism occurs when penicillin and aureomycin are given simultaneously in single doses. The Cooper strain of Type-I pneumococcus used was maintained in tryptase–phosphate broth at *p*H 7·4 containing 2% sheep erythrocytes, maximum virulence being obtained by serial passage in mice. For inoculation into these animals dilutions of 18-hour blood broth cultures were made in 0·85% sterile saline, the dose being determined by plate count. The minimum lethal dose was found to be 10 to 100 organisms, and 50 to 45,000 such doses were used to produce the experimental infection. Deaths and survivors were counted daily for 5 days. Aureomycin hydrochloride with sodium glycinate was diluted in sterile saline immediately before use, and crystalline benzylpenicillin was dissolved in sterile saline and stored at −20° C., individual tubes being thawed as needed. Combinations of these 2 drugs in various doses were administered to groups of 20 mice as follows: (1) before infection and mixed before injection; (2) before infection and injected separately; (3) concurrently at 2 or 6 hours after infection; (4) aureomycin 2 or 6 hours after infection, followed 4 hours later by penicillin; and (5) penicillin 2 hours, and aureomycin 6 hours, after infection. An equal number of mice were given each antibiotic alone in the same dose and at the same time-interval as it was given in each combination.

With both agents, used alone, there was a direct correlation between the dose and the percentage of mice surviving for 5 days in the 5 to 80% protective range, the survival rate increasing as an arithmetical function of the dose of aureomycin and as a logarithmic function of the dose of penicillin. When the effect on the protective activity of each drug of its combination with the other was studied it was found to vary according to circumstances, being additive in some experiments and antagonistic in others. The size of the inoculum was not a significant factor in determining this effect, which appeared to depend on the relation between the degree of protection afforded by each component acting separately.

The findings are shown in 4 diagrams. In the first the effect produced on the protective activity of increasing doses (0 to 10,000 units) of penicillin by giving a constant dose (0·05 mg.) of aureomycin 4 hours before is shown; aureomycin is antagonistic to penicillin throughout, but more so when the dosage of penicillin is at its most protective level (about 7,500 units) when used alone. In the second diagram the effect of increasing doses (0·02 to 1 mg.) of aureomycin given 4 hours before a constant submaximal protective dose (7,500 units) of penicillin is shown; the effect of aureomycin is additive initially, then becomes antagonistic until a level is reached at which it begins to be effective alone (0·5 mg.), when it once more becomes additive. The third diagram shows that penicillin in any dose tends to increase the proportion of survivors above that obtained with a poorly protective dose (0·5 mg.) of aureomycin alone, while the fourth diagram shows that the addition of a protective dose (7,500 units) of penicillin increases the protective effect of any dose of aureomycin between 0·1 and 1·0 mg., but to a diminishing extent as the dose of aureomycin (and its effectiveness given alone) increases.

Thus when a dose of penicillin which is highly protective alone against pneumococcal infection in mice is combined with a dose of aureomycin which alone is relatively non-protective, an antagonistic effect is likely, whereas when the relative effectiveness of the two doses is reversed, the combination of the two drugs is likely to give more protection than either alone.

Malcolm Woodbine

1525. **Penicillin Anaphylaxis, Nonfatal and Fatal Reactions**

S. M. FEINBERG, A. R. FEINBERG, and C. F. MORAN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **152**, 114–119, May 9, 1953. 12 refs.

Severe and even fatal reactions to penicillin are occurring with increasing frequency. The literature contains a large number of reports of severe reactions, but these certainly represent only a fraction of the anaphylactic reactions that actually occur. In this paper from the Allergy Research Laboratory, Northwestern University, Chicago, 9 cases are reported, of which 5 were fatal. The major symptoms are urticaria, asthma, shock, cyanosis, and unconsciousness. The onset is usually very rapid, and occurs a few seconds to several minutes after administration of the drug. In the fatal cases reported (in which the antibiotic was given intramuscularly) death appeared to result from shock or asphyxia. It is thought that probably any type of penicillin, administered by any route, can produce this reaction, which occurs more frequently in persons who are subject to other allergies, and is usually induced by repeated courses of penicillin.

For the prevention of this serious allergic hazard the following recommendations are proposed. (1) Penicillin should not be given for trivial conditions. (2) Before

the drug is administered the patient should be questioned about his allergic status, previous doses of penicillin, and any unusual reactions to it. (3) If there is any doubt, a skin test should be made, and if this gives a positive result the administration of penicillin should be avoided. The skin test is performed by placing a drop of crystalline penicillin solution (50,000 to 100,000 units per ml.) on a scratch, or a speck of the powdered drug dissolved in a drop of water or saline solution may be used. The appearance of a weal in 5 to 20 minutes indicates a positive reaction. If the scratch test is negative an intradermal test may be made, using about 0·01 ml. of a solution containing 100 units per ml. If this is also negative the concentration may be increased to 1,000 units per ml., but this should only be tried when the weaker solution has given a negative result. It is pointed out that a negative reaction is no indication that a delayed reaction of the serum-sickness type will not occur. In an acute attack adrenaline followed by aminophylline should be administered, and other supportive measures taken as necessary. *A. W. H. Foxell*

1526. **Effectiveness of Penicillin Administered Orally at Intervals of Twelve Hours**
N. N. HUANG and R. H. HIGH. *Journal of Pediatrics* [*J. Pediat.*] **42**, 532–536, May, 1953. 4 refs.

A series of 308 cases of common infections in infants and children was studied to evaluate the effectiveness of penicillin administered orally at intervals of 4 and 12 hours. Patients who received 300,000 units of penicillin at intervals of 12 hours responded as satisfactorily as did those who received 200,000 units as the initial dose followed by 100,000 units at intervals of 4 hours.

The effectiveness of procaine penicillin was comparable to that of potassium penicillin-G, when each was administered in equivalent amounts at intervals of 12 hours. —[Authors' summary.]

1527. **An Antiviral Substance from *Penicillium funiculosum*. I. Effect upon Infection in Mice with Swine Influenza Virus and Columbia SK Encephalomyelitis Virus**
R. E. SHOPE. *Journal of Experimental Medicine* [*J. exp. Med.*] **97**, 601–625, May 1, 1953. 4 refs.

In investigations carried out at the Rockefeller and Merck Institutes, New Jersey, a substance present in cultures of *Penicillium funiculosum* was found to be therapeutically effective against swine influenza virus infections in mice. During the course of the experiments, however, the mould gradually lost the property of elaborating this substance, but another substance, helenine, isolated from the same cultures, was found to be effective against Columbia SK encephalomyelitis virus infections in mice.

Helenine is present in the fluid of stationary cultures of *P. funiculosum*, but to a still greater extent in the cellular pellicles. It is extracted by mechanical bruising and precipitation from aqueous solution by 50% acetone, in which it is insoluble. A favourable response in infected mice depends upon treatment within 10 hours of infection, and little benefit is observed if treatment is delayed beyond 24 hours. Helenine exerts no effect if given when the mice already show signs of illness. An optimum dosage level is demonstrable, above which there is no further therapeutic benefit. Furthermore, helenine is not effective against massive amounts of virus, and the best results are seen in mice infected with 10 to 100 fatal doses of virus. The mechanism of its action is unknown, but it appears to be virustatic rather than virucidal, either inhibiting multiplication of the virus or interfering with its neuroinvasiveness. An additive therapeutic effect was observed between helenine and specific antiviral serum. *D. Geraint James*

1528. **An Antiviral Substance from *Penicillium funiculosum*. II. Effect of Helenine upon Infection in Mice with Semliki Forest Virus**
R. E. SHOPE. *Journal of Experimental Medicine* [*J. exp. Med.*] **97**, 627–638, May 1, 1953. 4 refs.

Helenine [see Abstract 1527] was injected intraperitoneally into mice infected subcutaneously with Semliki Forest virus and was shown to exert a favourable therapeutic effect if given within 18 hours of infection. A dosage–response curve similar to that obtained with Columbia SK encephalomyelitis virus infections was observed, effectiveness increasing until an optimum level was reached. The action of helenine against Semliki Forest virus would seem to be both to delay neuroinvasion and to kill the virus, frequently so rapidly as to prevent the acquisition of immunity by the cured mice. *D. Geraint James*

1529. **An Antiviral Substance from *Penicillium funiculosum*. III. General Properties and Characteristics of Helenine**
R. E. SHOPE. *Journal of Experimental Medicine* [*J. exp. Med.*] **97**, 639–650, May 1, 1953. 4 refs.

Helenine [see Abstracts 1527–8] loses its therapeutic activity gradually at room temperature. It keeps fairly well at refrigerator temperature, but is best stored under solid carbon dioxide. It is inactivated by boiling and by autoclaving at a pressure of 15 lb. per sq. in. (1·05 kg. per sq. cm.) for 15 minutes. It is filterable through a Seitz pad but is not dialysable. Whereas freeze-drying does not affect the activity of crude preparations of helenine, acetone-precipitated helenine is inactivated if it has been reconstituted in distilled water, but not when reconstituted in broth medium. Glucose and yeast extract may be the constituents of broth responsible for this protective effect.

Helenine, unlike specific antiserum, prevents the development of an immunological response by the infected host, presumably owing to destruction of virus antigen, possibly at an earlier stage of virus multiplication than that at which antiserum is effective. The chemical nature of helenine is unknown, but the crude active preparations contain a large proportion of polysaccharide. *D. Geraint James*

1530. **Thioaurin, a New Crystalline Antibiotic**
W. A. BOLHOFER, R. A. MACHLOWITZ, and J. CHARNEY. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **3**, 382–384, April, 1953. 2 refs.

Infectious Diseases

1531. **Betaine and Glycocyamine in Treatment of Poliomyelitis**
A. L. WATKINS. *New England Journal of Medicine* [*New Engl. J. Med.*] **248**, 621–623, April 9, 1953.

Nine patients with residual weakness one or two years after an attack of poliomyelitis and 1 after infectious polyneuritis were studied to determine the effect of betaine and glycocyamine on muscle strength.

Muscle strength was measured by means of standardized testing technics for the break resistance required for a variety of muscle actions as measured in pounds with a calibrated gauge instrument recording strain. Only 26% of the muscles tested showed as much as a 20% increase in strength, which did not appear significant subjectively or functionally. When increases in strength occurred they appeared in muscles that had not received intensive exercise to increase power.

Under the conditions of this study betaine and glycocyamine were not considered to have significant value in the treatment of muscle weakness as a residuum of poliomyelitis.—[Author's summary.]

1532. **The Clinical and Pathological Characteristics of Influenza.** (Материалы к клинико-лабораторной характеристике гриппа)
F. G. EPSHTEIN. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **31**, 31–41, Jan. 1953.

An outbreak of influenza due to virus A in the spring of 1949 provided the material for this analysis of the clinical and laboratory findings. Comparison with similar data from previous epidemics (1940 (Type B), 1943–4 (Type A), 1946 (Type A), and 1946–7 (Type B)) led the author to conclude that there is no reason to regard type-A influenza as more deadly than that due to virus B, and that it is impossible to distinguish between them clinically. [The epidemic in question, however, appears to have been a severe one, although no fatalities are reported. The total number of cases under observation is not mentioned and only percentages are given, which makes it difficult to evaluate the results.] Of the total, 7% of cases were classified as mild, 85% as of moderate severity, and 8% as severe; 18% occurred in persons under 18, 45% in those between 18 and 30, 24% in the age group 31 to 45, and 13% in those over 45 years of age. As to onset, 95% of patients started with a rigor, 93% complained of headache, 93% of cough, 87% of coryza, 73% of hoarseness, 80% of pain in the eyes or of conjunctivitis, 25% of herpes, and 15% of insomnia. On urinary examination, 64% were found to have haematuria and 35% had a trace of albumin. Leucopenia was found in 27% of cases on the first day, and in 63% of cases on the third day of the disease.

The most valuable diagnostic aid was provided by the cytological examination of swabs from the nasal mucous membrane. In the first 2 days of illness, 92% of such smears showed desquamated cylindrical epithelial cells. In other acute nasal infections the percentage of positive findings did not exceed 16%. In 82% of the cases antibodies were found in the serum; the titre increased four-fold in 32% of cases, and up to 32-fold in 4%. On the other hand 7% of the patients, who exhibited clinically all the symptoms of influenza, showed no antibodies from first to last. The duration of the illness was roughly inversely proportional to the initial antibody titre; in cases with titres of 1 : 160 or over the fever lasted less than 3 days and the disease less than 6 days, whereas none without initial antibodies recovered in so short a period.

The author also observed a number of sporadic cases of influenza which occurred both before and after the epidemic. These also were due to virus A, but the onset was less sudden and the course of the disease less severe; for example, rigors were much less common and eye symptoms occurred in only 34% of cases as against 80% during the epidemic. Whereas a history of contact could be established in 63% cases during the epidemic, in only 5% could this be done in the sporadic cases. The cytological examination of nasal swabs for cylindrical cells showed these to be present in only 53% of the sporadic cases.

During the epidemic, 42% of patients suffered from either bronchiolitis or pneumonia, but the course was benign and only one patient developed a pulmonary abscess. The author found " acrichin " (mepacrine) the drug of choice in treating these cases, 0·1 g. being given three times a day during the febrile period and for not more than one day thereafter; later, 0·3 g. was given in one dose on the first day, and then 0·1 g. three times a day for a further 1 or 2 days. *L. Firman-Edwards*

1533. **Epidemic Haemorrhagic Fever. 40 Cases from Korea**
R. ANDREW. *British Medical Journal* [*Brit. med. J.*] **1**, 1063–1068, May 16, 1953. 3 refs.

The author reviews the epidemiology, symptoms, and pathology of epidemic haemorrhagic fever and discusses its aetiology, basing his experience on 40 cases of the disease incurred in Korea and treated at a base hospital in Japan. The disease, previously known to the Russians and Japanese in Manchuria, is believed to be transmitted by a mite (*Laelaps jettmari litzthum*) which is harboured by the field rodent *Apodemus agrarius*. The highest incidence of the disease was in the months of May, June, October, and November and among troops stationed in damp ground and near river banks, and particularly among those in close contact with pack animals.

In the cases observed the onset was sudden, with chills, headache, and anorexia on the first day. By the third day vomiting had become a prominent symptom; sore throat and dizziness were noted in some cases. As the

disease progressed abdominal pain in the right upper quadrant became the most frequent complaint, and this, since it was associated with vomiting, often led to a diagnosis of acute infective hepatitis or even intestinal obstruction being made. Most of the patients reported sick on the third day, when the average temperature was 102·6° F. (39·2° C.). The period of fever averaged 5·5 days but the range was wide; in 2 cases it lasted only 3 days, while in 9 others it continued beyond the 7th day. The fever fell by lysis or crisis and did not relapse. The haemorrhagic lesions, from which the fever derives its name, included petechiae in the skin, which were observed in all cases from the third to the tenth day. Haemorrhages occurred into the conjunctiva and sublingual mucosa, and signs of haemorrhage into the gastro-intestinal, respiratory, and urinary tracts were also observed. Epistaxis occurred in 12 cases. In the one case which came to necropsy there were petechial or frank haemorrhages in all the viscera. Albuminuria was a constant finding and was accompanied by either macroscopic or microscopic haematuria. The blood pressure was normal in the early stages but rose later. The blood urea content rose to high figures, especially when vomiting was severe. Leucocytosis, with absolute increase in polymorphonuclear leucocytes, was constant after the third day; leucopenia was seen in only one case.

Treatment consisted in replacing by gastric drip the fluids and electrolytes lost by vomiting. No attempt was made to give fluids in the anuric or oliguric stages. The usual antibiotics appeared to be of no avail. Only one patient in the series died. Recovery was slow; in many cases the ability of the kidneys to excrete a concentrated urine took over 3 months to return to normal. Discussing the aetiology, the author points out the resemblance of the disease to a non-icteric form of Weil's disease, and suggests that the causative agent may be a leptospira. *William Hughes*

1534. **The Clinical Polymorphism of Infectious Mononucleosis.** (Le polymorphisme clinique de la mononucléose infectieuse)
R. Crosnier, A. Darbon, J.-F. Dulac, F. Quilichini, P. Doury, and M. Simon. *Annales de médecine* [*Ann. Méd.*] **54**, 187–213, 1953. 8 refs.

1535. **Herpes Simplex. A Study of Complement-fixing Antibodies at Different Ages.** [In English]
A. Holzel, G. V. Feldman, J. O'H. Tobin, and J. Harper. *Acta paediatrica* [*Acta paediat. (Uppsala)*] **42**, 206–214, May, 1953. 1 fig., 21 refs.

1536. **Herpangina: Clinical and Laboratory Aspects of an Outbreak Caused by Group A Coxsackie Viruses**
L. P. Kravis, K. Hummeler, M. M. Sigel, and H. I. Lecks. *Pediatrics* [*Pediatrics*] **11**, 113–119, Feb., 1953. 10 refs.

The authors discuss the relationship between Group-A Coxsackie viruses and herpangina and describe an outbreak of this illness in Philadelphia during the summer of 1951. Group-A Coxsackie viruses of three different types were isolated from stools and/or throat swabs obtained from 17 of 21 patients involved in the outbreak. In 3 patients a rise in complement-fixing and neutralizing antibody titres against homologous virus strains was demonstrated during convalescence. Asymptomatic carriers of this virus were detected, and it seems possible that 2 of the affected children acquired their infection from such a carrier.

It is considered that for laboratory confirmation of the diagnosis of herpangina recovery of virus from the throat lesions is necessary. In the absence of virus in the throat, the presence of virus in the stools or a rising antibody titre is not considered diagnostic. *Peter Story*

1537. **A Long-term Evaluation of Aureomycin in the Treatment of Actinomycosis**
L. V. McVay and D. H. Sprunt. *Annals of Internal Medicine* [*Ann. intern. Med.*] **38**, 955–966, May, 1953. 5 figs., 31 refs.

In 1949 the authors began a study of the effectiveness of aureomycin therapy in actinomycosis, since even with penicillin and sulphonamides the mortality and morbidity of the infection remained significant. Of the 10 cases observed during a period of 3 years at the John Gaston Hospital and University of Tennessee College of Medicine, Memphis, 5 have been followed up for more than 2 years after cessation of treatment with aureomycin. In 3 of the 4 cases of localized cervico-facial involvement the infection followed dental extraction; the remaining patient had hepatic actinomycosis. In a sixth case, observed only for 6 months, infection arose after head injury. In none of these cases was there any evidence of relapse during the period of follow-up, and the immediate clinical response in all instances was very satisfactory.

Two of the cases are described in detail. The first was in a coloured woman of 55 who had the cervico-facial type of infection; this had been present for 6 weeks before her admission to hospital and had not responded to treatment with penicillin and sulphonamides. Improvement was progressive when aureomycin to a total of 84 g. was administered over a period of 5 weeks.

The second case is that of a 60-year-old male negro (the 7th case treated with aureomycin) in whom generalized infection and haemorrhagic nephritis complicated the original cervico-facial actinomycotic lesion. He was treated with penicillin, dihydrostreptomycin, and aureomycin, and the latter antibiotic was also used with streptokinase and streptodornase for the local treatment of a large ulcerated area. The haematuria which had been a feature of the illness cleared up during the course of 5 to 6 weeks' treatment.

The authors are of the opinion that actinomycosis should be considered in the differential diagnosis of all subacute and chronic infectious processes of doubtful aetiology. They conclude that aureomycin, in doses of 750 mg. by mouth every 6 hours for 10 days and thereafter 500 mg. every 6 hours for 18 days, is effective in the treatment of cervico-facial lesions, and consider that a follow-up period of 5 years is probably not too long for such cases. *T. Anderson*

Tuberculosis

DIAGNOSIS AND PROPHYLAXIS

1538. **Clinical Evaluation of the Hemagglutination Reaction**

A. G. HOLLANDER, M. FROBISHER, and K. KALISCH. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] 67, 497–502, April, 1953. 3 refs.

The serum of 347 patients in the Veterans Administration Hospital, Atlanta, Georgia, all suffering from clinically active pulmonary tuberculosis, was tested for haemagglutinins in the hope of establishing a correlation between various aspects of the disease (duration, extent, progress, influence of cavitation, and effect of antimicrobial therapy) and the haemagglutination titre. About two-thirds of the patients had disease of more than one year's duration, and in more than half the total patients it was already far advanced, cavitation being recorded in 241 of them.

The Rothbard modification of the Middlebrook–Dubos reaction was used, serum dilutions ranging from 1 in 4 to 1 in 256 being prepared and, from laboratory experience, a titre of 1 in 16 chosen as a criterion of diagnostic significance.

The results were disappointing. In 58 cases (17%) the reaction was negative. In those cases in which haemagglutination occurred no significant correlation was found between the height of the titre and any other characteristic studied except the presence of excavation. Of the cases with cavitation 62% had a titre of 1 in 16 or more, as compared with 44% of those without cavitary disease.

The authors suggest that their findings justify further investigation, and also express the hope that modifications leading to the production of a more sensitive antigen may be developed in the future. *R. J. Matthews*

1539. **Killed Vaccine with Diffusing Factor (V.D.S.) in the Prophylaxis of Tuberculosis in Man.** (Il V.D.S. nella vaccinazione antitubercolare profilattica nell'uomo)

G. SALVIOLI. *Minerva medica* [*Minerva med. (Torino)*] 44, 1313–1320, May 19, 1953. 15 figs.

The author describes his experience at the Paediatric Clinic, Bologna, in the prophylactic treatment of children for tuberculosis by the intradermal injection of a heat-killed vaccine to which hyaluronidase was added. The latter causes diffusion of the vaccine through a larger skin area and, in the author's opinion, enhances the immunizing effect. The vaccine is prepared by suspending fresh cultures of human (70%) and bovine (30%) bacilli in physiological saline so that 1 ml. contains 3·75 mg. of bacilli. This is then heated at 100° C. for 10 minutes. After cooling to room temperature, hyaluronidase is added in the porportion of 30 " U.V." [presumably 30 turbidity-reducing units] per ml. The lyophilized vaccine is put up in 1-ml. ampoules and will keep for 2 years. The dose used for infants under 1 year was 0 · 2 ml and for children above this age 0·1 ml.

The local reaction consists first of a nodule, which lasts from 2 to 4 months. This may be followed by further inflammation and ulceration, especially in older children. Reabsorption and scarring occur in 6 months to 1 year. In those inoculated after puberty the reaction tended to be prompter, appearing in 6 to 7 weeks, and the inflammation and ulceration were more pronounced. Occasionally, in the absence of any local reaction, evidence of tuberculous allergy may appear elsewhere. Histological examination of the nodule in one case showed typical tuberculous inflammation, with round-cell infiltration and central caseation with Langhans giant cells.

Altogether 334 children have been vaccinated by this method so far. Mantoux testing at 6, 12, and 18 months after vaccination gave positive reactions in 85 to 100% in the different age groups. The author considers that the results of using this heat-killed vaccine are superior to those obtained with B.C.G. *D. Weitzman*

TUBERCULOUS MENINGITIS

1540. **Tuberculous Meningitis in the Adult. A Review of Sixty Consecutive Streptomycin-treated Cases**

E. A. RILEY. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] 67, 613–628, May, 1953. 1 fig., 39 refs.

The results of treatment of 60 consecutive cases of tuberculous meningitis in adults at the Bellevue Hospital, New York, with streptomycin between 1946 and 1951 are described. All the patients received streptomycin or dihydrostreptomycin intramuscularly, and the majority also received these drugs intrathecally. [The duration of treatment is not clearly stated.] Of the 60 patients, 3 were lost to follow-up and 53 died.

The author considers that the prognosis in this disease is worse in adults than in children, and is especially poor when the meningitis occurs as a complication of an active tuberculous focus in another part of the body. It is stated that 25 of the patients, all of whom died, had received streptomycin or dihydrostreptomycin before the onset of the meningitis; in these patients streptomycin-resistant organisms were presumed to be present in the meninges. *R. H. J. Fanthorpe*

1541. **Clinical Diagnosis of Tuberculous Meningitis in Adults.** (К клинике туберкулезного менингита у взрослых)

C. I. ROTENBERG. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] 31, 40–44, April, 1953. 1 fig., 8 refs.

The author has based his conclusions on a series of 14 cases of tuberculous meningitis in adults aged from 37 to 72 years, of whom 6 were over 50. In 8 of them

there was a history of miliary tuberculosis, and half of the patients suffered from tuberculous disease of the urogenital system.

Tuberculous meningitis in adults is characterized by the following features: (1) acute onset and progress of the disease (the maximum duration was 26 days); (2) predominance of cerebral over meningeal symptoms, and the frequency of psychological disturbances; (3) the rarity, as compared with the disease in childhood, of basal symptoms, epileptiform convulsions, and general hyperaesthesia. In 4 cases in this series the onset was suggestive of cerebral haemorrhage, and in only 4 others were there premonitory symptoms—the rest were of acute development. In 3 cases meningeal symptoms were absent and in 5 others very slight, in 11 cases there was headache, but in only 7 was this intense; cranial-nerve disturbances were observed in only 2 patients. In only 2 cases were there epileptiform convulsions, and in both, post-mortem examination revealed a tumour of the brain, a meningioma in one case, and a cavernous angioma in the other.

Changes in the cerebrospinal fluid were variable; generally, there was increase in the protein content, and the cell content was high, but in a number of cases there was no correlation between these findings, so that the ratio of protein content to the number of cells was inconstant. In 3 cases there was xanthochromia, and in 3 cases neutrophil leucocytes predominated in the cell count; tubercle bacilli were found in only one case. There was no parallelism between the degree of cytosis and the severity of symptoms. The blood leucocyte count was raised in 6 cases, but in most only slightly. The differential diagnosis is often difficult and must be based on a history of tuberculosis, the sudden onset and serious course of the disease, and a knowledge of the peculiarities of meningitis in adults, especially the dissociation of the protein:cell ratio in the spinal fluid.

L. Firman-Edwards

RESPIRATORY TUBERCULOSIS

1542. **The Surgical Treatment of Pulmonary Tuberculosis**
G. CRUICKSHANK. *Edinburgh Medical Journal* [*Edinb. med. J.*] **60**, 201–211, May, 1953. 15 figs., 2 refs.

From his experience at the Leicester Chest Unit, the author discusses the present position of surgery in the treatment of pulmonary tuberculosis. Thoracoscopy for adhesion section and phrenic crush are briefly mentioned, the author employing phrenic crush with a pneumoperitoneum as a temporary "cooling-down" measure rather than as a definitive method of treatment. His experience of extrapleural pneumothorax is small, but he uses it either as a preliminary to thoracoplasty in cases in which there is no fibrosis, or to control disease on one side when a pneumothorax is unobtainable and a thoracoplasty is planned on the other. Late tuberculous infection in the extrapleural space is still a problem, however.

Thoracoplasty gives good results in cases of apical disease with a tendency to fibrosis but without atelectasis or marked bronchiectasis. This operation is preferred to resection in the presence of contralateral or extrapleural pneumothorax. The method of choice is a 7-rib thoracoplasty in three stages under local analgesia.

The indications for lung resection given by the author are those now widely accepted. In his series of 100 cases, 102 resections were carried out, in 26, the largest group, for "anticipated thoracoplasty failure". (The author states that anticipation of failure was based on experience gained from the follow-up study of cases in which thoracoplasty was performed by various surgeons over the previous 10 years.) Among the 26 cases in this group were some with giant cavity, bronchiectatic upper lobe, pectoral segment cavity, and extension of the disease into the lower lobe. In 60 cases in which pneumonectomy was performed there were 4 early and 2 late deaths, and the sputum of 53 of the 60 patients was negative for at least one year. In 42 cases of lobectomy there were 2 deaths, the sputum being negative in 36. There were 6 cases of bronchopleural fistula in the whole series. In 19 cases thoracoplasty was carried out 5 to 8 weeks after pneumonectomy; as a result of experience in these cases the author now prefers, when possible, to perform thoracoplasty and pneumonectomy in one procedure.

A. M. Macarthur

1543. **Thoracoplasty and Resection for Pulmonary Tuberculosis**
F. A. HUGHES, C. C. LOWRY, and J. W. POLK. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **25**, 454–467, May, 1953. 2 figs., 23 refs.

The authors report the results in 235 patients with pulmonary tuberculosis treated between January, 1947, and October, 1951, at Kennedy Hospital (Veterans Administration), Memphis, Tennessee, of whom 111 were treated by thoracoplasty and 124 by resection. Follow-up details were obtained from 6 months to 5 years after the time of the operation.

A comprehensive comparison between the two groups of cases is made. [Unfortunately, the indications for one or other operation are not defined, but it would appear that the two groups are not comparable. Thus much of the value of this communication is lost.] For what they are worth the results in the group undergoing resection were slightly more favourable in most respects (operative mortality, late mortality, operative and late spread of the disease), while in this group also the disease became inactive in a greater number of cases and more patients have returned to work. *W. P. Cleland*

1544. **The Use of Suture Constriction of the Upper Lobe in the Treatment of Pulmonary Tuberculosis (Paulino Procedure)**
P. T. DECAMP, T. G. BAFFES, J. W. OVERSTREET, and A. OCHSNER. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **25**, 219–233, March, 1953. 9 figs., 5 refs.

The authors describe their experience at the Charity Hospital, New Orleans, of a modified type of one-stage thoracoplasty operation which was originally devised by Paulino of Rio de Janeiro. In this operation the whole of the 1st and 2nd ribs, and shorter lengths of the 3rd

and 4th ribs are resected subperiosteally as far posteriorly as the transverse processes. An extrafascial pneumonolysis, with division of the intercostal bundles anteriorly and posteriorly, is performed to a level below the diseased part of the lung. On the mediastinal side mobilization is carried down to the level of the hilum. Three horizontal encircling purse-string sutures of No. 10 crochet cotton are placed around the lung so as to produce concentric collapse and compression; these ligatures also prevent subsequent re-expansion. The indications and contraindications for, and advantages of, this type of operation are essentially the same as those observed in plastic-ball plombage.

During the last 2½ years, 34 operations have been performed on 31 patients (3 bilateral operations). Of the 31 patients, 17 were over the age of 40 years. There were no complications attributable to the use of the encircling ligatures, and follow-up investigation of 25 patients more than 7 months later revealed sputum conversion and cavity closure in 18. *R. L. Hurt*

1545. **Treatment of Chronic, Predominantly Fibrotic Pulmonary Tuberculosis with Isoniazide ("Isocotin Nyco"). A Controlled Study**

S. Eggen, A. Klingenberg, E. Refsum, A. Tuxen, and H. J. Ustvedt. *Journal of the Oslo City Hospitals* [*J. Oslo City Hosp.*] **3**, 115–126, May, 1953. 1 fig.

The efficacy of isoniazid in the treatment of chronic pulmonary tuberculosis was studied at Vardåsen Sanatorium and Ullevål Hospital, Oslo. The drug was given in doses of 200 mg. daily for 12 weeks to 30 patients, all of whom had had fibrotic cavernous pulmonary tuberculosis for several years which was not amenable to surgery, and in whom there were, at the most, only slight toxic symptoms; 20 similar patients serving as a control group received an inert drug disguised as isoniazid. Two of the treated patients and one of the control group were, however, lost to follow-up.

The results [which are similar to those reported by the Tuberculosis Chemotherapy Trials Committee of the Medical Research Council (*Brit. med. J.*, 1952, **2**, 735; *Abstracts of World Medicine*, 1953, **13**, 195)] were as follows: (1) isoniazid had a definite antituberculous activity; (2) it had no great effect upon the patient's weight and appetite; and (3) resistance to isoniazid rapidly developed, precluding use of the drug by itself. *John Sumner*

1546. **The Effect of Streptomycin on the Emergence of Bacterial Resistance to Isoniazid**

United States Public Health Service Cooperative Investigation. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **67**, 553–567, May, 1953. 3 figs.

The development of increased bacterial resistance to isoniazid has now been frequently observed. Because of the wide interest in the possibility of reducing the frequency of this phenomenon by combining isoniazid with streptomycin in the treatment, the results of this investigation (compiled at the Field Research Branch of the Division of Chronic Disease and Tuberculosis, U.S. Public Health Service, on behalf of 30 clinical investigators and 22 hospitals) are now published, though it is stressed that they should be regarded as provisional and preliminary.

Three regimens of treatment were employed—namely, streptomycin with PAS, streptomycin with isoniazid, and isoniazid alone, the dosage being: streptomycin 1 g. twice weekly, PAS 10 to 12 g. per day, and isoniazid 150 to 300 mg. per day. Some 1,500 cases were observed and the investigation extended over 64 weeks—that is, 40 weeks of chemotherapy and a further 24 weeks of observation. The drug susceptibility of cultures was determined uniformly by testing centrally. However, as it was impossible to examine frequent cultures from 1,500 patients, cultures from all the patients were examined at the beginning and end of treatment, and information on changes occurring during treatment was obtained by sending all cultures from all patients in 5 of the hospitals to the Trudeau Sanatorium laboratories, New York, at 4-weekly intervals for testing. Organisms were considered streptomycin-resistant if they grew in a concentration of 10 μg. of the antibiotic per ml. within 5 weeks. No similar criterion was possible with isoniazid, but inspection revealed that less than 50 colonies grew in the presence of 0·1 μg. of isoniazid per ml. in pre-treatment cultures and there was no growth in higher concentrations. For the present studies, therefore, growth in inoculated cultures was defined as the appearance of at least 50 colonies after 5 weeks' incubation.

Results, depicted graphically, of cultures of 4-weekly samples of sputum show that the percentage of positive cultures continued to decrease after 12 weeks only in patients receiving both streptomycin and isoniazid. After 28 weeks, the percentages of positive cultures were for patients given streptomycin and isoniazid 24%, streptomycin and PAS 36%, and isoniazid alone 49%. In patients with streptomycin-susceptible organisms initially, the comparable figures were 11%, 27%, and 42% respectively. Results of isoniazid-susceptibility tests showed that at 12 weeks, 13%, 18%, and 18% of cultures showed growth in 0·1, 1·0, and 5·0 μg. of isoniazid per ml. respectively, the figures being 7%, 16%, and 25% at 28 weeks. With the combination of streptomycin and isoniazid, the reduction in frequency of positive cultures continued for 16 to 20 weeks. Whereas of those patients given isoniazid alone, about half showed tubercle bacilli in the sputum, only about a quarter of those receiving both drugs did so. By the 28th week all positive cultures exhibited growth in some concentration of isoniazid. It is emphasized that resistance to isoniazid appears much less frequently if patients are treated with both drugs, but that pre-treatment status is related to susceptibility, and the presence of cavities markedly increases the number of positive cultures obtained at 28 weeks.

The emergence of streptomycin-resistant organisms in the additional presence of either isoniazid or PAS was also studied. With streptomycin and isoniazid 11% of cultures were positive at 20 weeks, 4 to 7% being resistant to 10 μg. of streptomycin per ml. and 7% resistant to 100 μg. With streptomycin and PAS the development of streptomycin resistance was much more marked, growth in a concentration of 10 μg. per ml. being seen

in 10% at the 4th week, increasing to 17% at the 28th week, with 7% resistant to 100 μg. per ml. after 28 weeks.

It is concluded that isoniazid is specifically more effective than PAS in preventing the emergence of organisms only moderately susceptible to streptomycin. When given isoniazid and streptomycin together only about 1 in 10 patients had tubercle bacilli in the sputum after 28 weeks, while of those given PAS and streptomycin approximately 3 out of 10 had positive sputum.

Malcolm Woodbine

1547. **Late Results of Modified Bed Rest in Active Uncomplicated Minimal Pulmonary Tuberculosis**

R. S. MITCHELL. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **67**, 401–420, April, 1953. 4 figs., 4 refs.

The author describes the results of a regimen of modified bed rest in 589 cases of active minimal pulmonary tuberculosis treated at the Trudeau Sanatorium, New York, during the period 1927–46 (including 307 such cases treated during the years 1930 to 1940 and previously reported by the author (*Amer. Rev. Tuberc.*, 1950, **61**, 809)). The patients in this series represent nearly half of the total number (1,196) classified on admission as having active minimal disease on admission to the sanatorium during these years. [Not all the exclusions are explained and the influence of selection is difficult to assess.] Modified bed rest is defined as " approximately twenty to twenty-one hours a day reclining in bed or on a chaise longue ", but it is admitted that there may have been wide variations in the interpretation of this and in other factors during the early years covered by the investigation.

In correlating results, the known histories of patients are supplemented by life-tables covering probable eventualities in those with whom contact was lost during life (about 10%) and those who died from uncertain causes (3% are computed to have died from tuberculosis and 4% from other causes). The effectiveness of treatment is then measured by means of 5-year progression rates, progression being defined as " any definite increase of disease or development of cavity interpreted from the chest roentgenogram "; most progressions were also confirmed in other ways. The cumulative life-tables showed that 201 (35·8%) of the 589 patients had at least one progression in the 20 years under survey; 60% of these occurred within a year of discharge from the sanatorium. Further progressions occurred in about one-third of those who had primary progressions, but many recovered and in 1951–2, 470 (80%) patients were recorded as being well and able to work, though the aggregate loss in economic usefulness had been considerable. The only factors which appeared to be related to the incidence of later progression were age—prognosis improved with age—and the extent (even within minimal limits) of the disease. Duration of modified bed rest or even of length of stay in hospital seemed unrelated or insignificant.

[The statistical methods employed, including the life-tables and the cumulative progression rates (used to eliminate time-phase, occupational, and other discrepancies) are ingenious, and overcome some of the difficulties of retrospective survey, but many potential fallacies remain. For example, 93% of patients admitted before 1936 were diagnosed because of symptoms, compared with only 53% so diagnosed after that year, a change due chiefly to the increase in the use of radiology. The author recognizes the controversy of " symptoms versus shadows ", and admits the difficulty of assessing personal factors in the treatment of cases during the earlier years. Treatment by graduated rest and exercise depends on the physician's control of the patient's systemic reaction, both of which are highly personal. The author rather deprecates the ultimate results, but if the cases were unselected it would seem more reasonable to doubt some of the intermediate conclusions. Even with " minimal " cases, to find 80% still capable of work after many years speaks well for the form of treatment employed.]

R. J. Matthews

1548. **Late Results of the Treatment of Primary Tuberculous Pleurisy with Effusion with Modified Bed Rest**

R. S. MITCHELL. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **67**, 421–431, April, 1953. 2 figs., 18 refs.

This is a complementary survey to that summarized above [Abstract 1547], and concerns the subsequent fate of the 194 patients who had pleurisy with effusion. Tubercle bacilli were found in the sputum or exudate in 71 (37%) of these cases. In the remainder the pleurisy was considered to be of tuberculous origin on clinical or radiological grounds and in the absence of other recognizable cause, but aspiration was not performed on 63 of them. Of 186 patients followed up for at least 5 years some (minimal) degree of pulmonary infiltration was observed in 76 (39%), none in 88, and in 22 cases it was undetermined. All the patients were white and their average age was 25·5 years.

Of the 167 patients with whom contact was maintained for the whole period, 142 (85%) were well and able to work 5 to 25 years later. Life-tables were compiled to cover mortality and loss of contact in the remainder, and by using these to supplement the information obtained directly, cumulative rates for the whole group were computed in order to assess the relationship between primary factors and ultimate results. The cumulative rate of reactivation of the disease in the 20 years covered was estimated at 24% (with many recoveries), 93% of these occurring in the first 5 years after discharge from the sanatorium. The cumulative mortality rate was 5%. The author concludes that the only single factor which appeared to influence prognosis in regard to reactivation was the degree of pulmonary infiltration, and that neither age, sex, symptoms, bacteriological findings, the duration of bed rest, nor length of sanatorium treatment had any apparent relation to the results.

[Over 80% of the patients had less than 6 months' modified bed rest, and about 30% less than 3 months'. The difficulty, therefore, of evaluating this factor, and also certain of the statistical methods used, may justify a little doubt as to some of the conclusions drawn from an otherwise excellent survey.] *R. J. Matthews*

Venereal Diseases

SYPHILIS

1549. **Results obtained with the von Boros Serum Reaction in Syphilis.** (Résultats de la nouvelle réaction syphilitique d'après V. Boros)
L. WOLFF and W. TEUSCH. *Annales de dermatologie et de syphiligraphie* [*Ann. Derm. Syph. (Paris)*] **80**, 151–160, March–April, 1953. 2 figs., 8 refs.

The technique of this flocculation test, introduced by von Boros in 1949, is described. Having employed the test in some 25,000 cases examined at the Institute of Hygiene, Saarbrucken, for the detection of syphilis, the authors found that it compared very favourably with the standard Kahn, Meinicke, and Wassermann tests; they conclude that its sensitivity, simplicity, and rapidity—the whole reaction takes only 50 to 60 minutes—give it great advantages over these other methods. The von Boros test can also be used for the examination of cerebrospinal fluid. *James Marshall*

1550. **A Study of the Neurath Inhibition Phenomenon in the Serodiagnosis of Syphilis**
V. H. FALCONE, A. HARRIS, S. OLANSKY, C. SALVADO, and J. C. CUTLER. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **37**, 264–272, May, 1953. 8 refs.

Among the methods devised to aid in differentiating between positive reactions to the serological tests for syphilis which are actually due to that disease and those produced by other conditions is the Neurath procedure, in which a heat-stable " inhibitor " fraction of serum is used. It is claimed that the false positive flocculation reaction is inhibited by the addition of the Neurath serum fraction, whereas the positive reaction due to syphilis remains unchanged.

At the Venereal Disease Research Laboratory of the U.S. Public Health Service, the present authors used the Neurath technique in a series of tests performed with three different antigens—two antigens of the cardiolipin–lecithin type as used for the V.D.R.L. and Rein–Bossak flocculation tests and a lipoidal antigen as used for the Mazzini flocculation test. At the same time standard Rein–Bossak, Mazzini, and V.D.R.L. slide tests were performed on the same sera without reference to the results of the Neurath tests. Specimens of blood for testing were obtained from sources which included the children of an orphanage in Guatemala City, in whom the incidence of congenital or acquired syphilis was low and malaria, a fruitful source of false positive reactions, was not present, and school-children in San José, Guatemala, where the incidence of malarial infection is very high. Blood from non-syphilitic and syphilitic adults was also included.

The results obtained with the Neurath procedure were shown to be dependent to a great extent on the type of antigen employed. In 108 specimens of blood from 100 syphilitic patients the proportion of negative reactions was considerably fewer with the Mazzini antigen than with the other two, but many of the positive reactions with the Mazzini antigen were of the " biologic " type, and only 39 (36%) of the syphilitic type, compared with 60 (56%) with the V.R.D.L. antigen and 77 (71%) with the Rein–Bossak antigen. There was little difficulty in detecting false positive reactions to tests by the routine method by: (1) the absence of history or clinical signs of syphilis; (2) the finding of discrepancy between the results of the various tests which were used, and even between results of the same test when repeated on the same individual; and (3) the absence in these cases of a progressive and sustained rise in serological titre or of agreement between the results of all the tests during the period of observation.

It was therefore concluded that the employment of the Neurath procedure added no significant information to that given by the standard serological tests under the circumstances in which this study was conducted.
A. J. King

1551. **Broad-spectrum Antibiotic Therapy of Early Syphilis. Posttreatment Survey**
H. M. ROBINSON and H. M. ROBINSON, Jr. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **37**, 243–246, May, 1953. 3 refs.

A follow-up survey was carried out at the University of Maryland School of Medicine on cases of early syphilis treated by the authors 2 to 4 years previously with chloramphenicol, aureomycin, or oxytetracycline (" terramycin ").

Of the 14 patients treated with chloramphenicol, one defaulted from observation, 2 had serological relapses, and one a mucocutaneous relapse; in 2 the serological test results were doubtful, in 3 they remained positive with titres of 1, 4, and 8 units respectively, and in 5 (30%) they remained negative and the spinal-fluid examination was also negative.

In the aureomycin-treated group 6 of the 10 original patients treated by the oral route were examined; of these, 5 were sero-negative and one was sero-positive with a titre of 2 units, but all were negative on spinal-fluid examination. Of 7 patients (out of 10) treated with aureomycin intravenously, one who had earlier been sero-negative had now become sero-positive, one still showed a positive titre of 4 units, and 5 (71%) had negative blood and spinal-fluid findings.

Of the group of 5 patients given oxytetracycline, one had died of pneumonia, one had a serological relapse, and in 3 serological tests and spinal-fluid examinations were negative. Although the series is admittedly small, the authors conclude that these three drugs are of value as antisyphilitic agents when penicillin is contra-

indicated, but prolonged surveillance is called for in view of the possibility of serological or clinical relapse.

Douglas J. Campbell

1552. **Treatment of Early Syphilis with Terramycin. Report Based on a Study of Ten Cases**

S. IRGANG and E. R. ALEXANDER. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **37**, 247–252, May, 1953. 13 refs.

The treatment of syphilis with penicillin has not been entirely satisfactory, an appreciable incidence of penicillin dermatitis and penicillin shock having been reported. For this reason the authors, working at Harlem Hospital, New York, have treated 10 cases of early acquired syphilis with oxytetracycline (" terramycin ") given orally. Irrespective of body weight, 2 g. a day (500 mg. 6-hourly) was given for 14 days, and the patients were observed for 12 weeks or longer.

Local and general Herxheimer reactions were encountered, one patient developed a mild dermatitis and another herpes simplex. *Treponema pallidum* was destroyed in surface lesions in from 44 to 96 hours; in most cases the cutaneous lesions responded favourably, but a few were slow in resolving. The effect on serological reactions was also favourable, though only 5 patients completed adequate post-treatment surveillance: of these, 2 were serologically negative within 12 weeks, but a third not until 7½ months. In one case resistance to oxytetracycline developed, with lack of proper healing response in the cutaneous lesions, and prolonged treatment was required to destroy the treponemes in the surface lesions.

The authors confirm the experience of other workers that oxytetracycline has treponemocidal properties and could be used when penicillin is contraindicated, but the dosage should exceed 2 g. per day and be continued for at least 2 weeks. They recommend that bismuth therapy should be given conjointly. *Douglas J. Campbell*

1553. **Ambulatory Treatment of Cardiovascular Syphilis with Penicillin**

J. EDEIKEN, H. BEERMAN, J. H. STOKES, and E. STANNARD. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **37**, 237–242, May, 1953. 14 refs.

The authors report, from the University of Pennsylvania, the results of the ambulatory treatment of cardiovascular syphilis with procaine penicillin. Of the 19 patients (6 with simple aortitis, 10 with aortic insufficiency without aneurysm, and 3 with aortic insufficiency and aneurysm), 4 showed symptoms of congestive heart failure. The dosage was either 9 mega units of procaine penicillin in daily doses of 600,000 units or 6 mega units of procaine penicillin with 2% aluminium monostearate, the patients attending as out-patients.

All 19 patients tolerated the course without untoward immediate reactions, except that one who was also suffering from neurosyphilis had fever after the first injection but was able to complete the course. In the authors' experience patients with involvement of the central nervous system often show reactions of a mild or even serious degree, so that the preliminary examination should also include examination of the spinal fluid. Surveillance was carried out at 3- and 6-monthly intervals. During the period of surveillance 2 patients died, but there was no evidence that treatment was in any way responsible for either death. From these results the authors conclude that penicillin may be safely administered to ambulatory patients. In no case did a Jarisch–Herxheimer reaction to penicillin develop.

Douglas J. Campbell

1554. **Important Details Concerning the Argyll Robertson Pupil**

C. D. BENTON. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **37**, 232–236, May, 1953. 5 refs.

The author reviews the features of the Argyll Robertson pupil—namely, irregularity, meiosis, loss of reaction to light, preservation of reaction on convergence, poor response to mydriatics, delayed response to eserine, and atrophy of the iris—and points out that the loss of the light reflex develops through definite stages which are the same as those of physiological fatigue in normal eyes. In incomplete Argyll Robertson pupil, however, impairment of the pupillary light reflex occurs in one or more segments rather than in the entire iris. The irregularity of the outline is due to structural changes rather than to a disturbance of innervation, for it persists after death.

Dealing with the frequency of this phenomenon the author recalls that in a study of over 400 cases of neurosyphilis Merritt and Moore (*Arch. Neurol. Psychiat. (Chicago)*, 1933, **30**, 357) found a complete Argyll Robertson pupil in only 45%. Theories about the location of the lesion responsible for the phenomenon are briefly discussed. A lesion of the periaqueductal grey matter would not explain the meiosis, irregularity, and diminished responsiveness to drugs, and the author therefore favours the theory of Langworthy and Ortega (*Medicine (Baltimore)*, 1943, **22**, 287) that the lesion is in the nerve fibres in or near the iris; the preservation of the reaction on convergence is attributed to the fact that this synkinetic movement is normally much stronger than the light reflex. In advanced cases the reaction on convergence is lost, as well as the light reflex.

J. Foley

1554. **The Effect of Adrenocortical Hormones on the Lightning Pains and Visceral Crises of Tabes Dorsalis. With Some Remarks on the Pathogenesis of Tabes Dorsalis**

J. E. MOORE. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **37**, 226–231, May, 1953. 1 fig., 9 refs.

The author draws attention to 5 cases of arrested tabes dorsalis with lightning pains treated at Johns Hopkins Hospital, Baltimore, in which cortisone or ACTH diminished the severity of the pains. In the one case which is described in full, cortisone was given for a period of over 8 months, and during this period and for about 4 months afterwards the duration and severity of the lightning pains were reduced by about 75%. Nine months after cessation of the treatment a Charcot's

arthropathy of a lumbar intervertebral joint appeared. In 2 of the other cases treated with the hormones there were gastric crises, which in one case improved; but as such crises are episodic to an even greater degree than lightning pains, the value of this method of treatment remains unproven. *J. Foley*

GONORRHOEA

1556. **Treatment of Gonorrhea with Erythromycin**
G. R. GABLE, M. J. ROMANSKY, and S. R. TAGGART. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **37**, 377–378, July, 1953. 4 refs.

Eleven strains of freshly isolated *Neisseria gonorrhoeae* were tested *in vitro* against erythromycin; 4 were sensitive to less than 0·1, 4 to 0·2, 1 to 0·3, and 2 to 0·4 μg. per ml. Ninety-six per cent of patients given 2·0 g. of erythromycin orally in either single or divided doses were cured. There was a decreasing percentage of cures with lesser amounts of the antibiotic (50% with 1·0 g., 23·3% with 0·5 g., and 25% with 0·3 g.).—[Authors' summary.]

1557. **The Treatment of Acute Gonorrhea in Male Patients with an Aureomycin–Triple Sulfonamide Combination**
L. T. WRIGHT and W. E. METZGER. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **37**, 259–263, May, 1953. 4 refs.

In view of recent reports that the antibacterial activity of aureomycin *in vitro* may be increased by combination with other agents, notably sulphonamides, a clinical trial was carried out at Harlem Hospital, New York, in which tablets containing 125 mg. of aureomycin and 167 mg. each of sulphadiazine, sulphamethazine (sulphadimidine), and sulphamerazine were used in the treatment of 70 cases of acute anterior gonococcal urethritis in the male. Earlier experience had shown that the minimum effective total oral dose of aureomycin alone was approximately 1·0 g., which gave a cure rate of 94·3% in 122 cases, whereas in a smaller number of cases a dose of 0·5 g. was ineffective.

In the authors' present series of cases four tablets were given to each patient—2 immediately, one 6 hours later, and one 12 hours later. This amounted to a total of 0·5 g. of aureomycin and 0·668 g. of each of the three sulphonamides. The cure rate was 94·3%, which was identical with that obtained with double the dose of aureomycin alone.

The authors conclude that the sulphonamides potentiate the activity of aureomycin against the gonococcus *in vivo*, and they claim for this method of treatment that it reduces the incidence of toxic effects and is more economical than the use of a larger dose of aureomycin alone. There are other possible advantages, namely: (1) that with the lower dose of the antibiotic the symptoms and signs of other venereal diseases, especially syphilis, are less likely to be masked; (2) that the combination of drugs may be effective in cases resistant to one drug; and (3) that the range of antibacterial activity of this preparation might be expected to be greater than that of aureomycin alone. On the other hand there is the danger that the use of small amounts of aureomycin might encourage the development of resistant bacteria in certain types of infection, although this is unlikely with acute gonorrhoea. *A. J. King*

LYMPHOGRANULOMA VENEREUM

1558. **Serology, Frei Reaction, and Epidemiology of Lymphogranuloma Venereum**
A. B. GREAVES and S. R. TAGGART. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **37**, 273–282, May, 1953. 2 figs., 18 refs.

The authors applied the Frei test and the complement-fixation test for lymphogranuloma venereum in the investigation of 200 patients attending a clinic organized by the Bureau of Venereal Diseases of the District of Columbia Health Department, Washington. All were negroes of low educational level and most were sexually promiscuous; the ages of the patients varied from 16 to 67 years.

Complement-fixation tests were first performed on the sera of 84 patients, of whom 45 had symptoms and signs suggestive of lymphogranuloma and 39 were presumed to be suffering from asymptomatic infection, although only 15 of them gave a past history of buboes. The mean quantitative titre (the reciprocal of the highest dilution of serum giving complete fixation of complement) was 80 for those patients with clinical evidence of the disease, 40 for those with history of bubo but no signs, and 20 for the remaining 24 with neither history nor signs. Application of the Frei test to 104 patients with positive serological reactions of varying titre showed no significant correlation between the serological titre and the presence or absence of a positive reaction to the Frei test or the size of such a reaction, while the proportion of positive Frei reactions was much the same in symptomatic and asymptomatic cases. A study of the serological titres in relation to the time since infection, as judged by the statements of patients with a past history of bubo, showed that complement-fixing antibody might persist in comparatively high titre (40) for as long as 20 years. There was, however, a tendency for the titre to diminish with time and also some indication that spontaneous reversal to negativity might occur. There was no evidence to indicate whether persistence of antibody pointed to latent infection; the possibility of reinfection could not be excluded in these cases. Examination and testing of contacts of some patients believed to be suffering from asymptomatic infection indicated that some of these patients were probably infectious. *A. J. King*

1559. **A Case of Granuloma Inguinale in Scotland: Response to Aureomycin**
A. G. FERGUSSON and G. B. S. ROBERTS. *British Medical Journal* [*Brit. med. J.*] **1**, 1257–1259, June 6, 1953. 4 figs., 20 refs.

Tropical Medicine

1560. **Terramycin in Cholera**
A. Das, S. Ghosal, A. Mondal, and S. K. Gupta. *Journal of the Indian Medical Association* [*J. Indian med. Ass.*] **22**, 268–271, April, 1953. 3 refs.

In a trial of " terramycin " (oxytetracycline) in cholera (*Indian med. Gaz.*, 1951, **86**, 437; *Abstracts of World Medicine*, 1952, **12**, 318) the authors found that the drug sterilized the faeces by the second day in 22 of 26 patients, but that the mortality was not affected as compared with a control series. It was felt, however, that in so acute a condition as cholera the efficacy of the drug might be greater when given as early as possible in the disease, and the present paper describes a further trial made during an epidemic in Calcutta in 1952. Altogether 357 cases were admitted to the Nilratan Sarkar Hospital, in 146 of which oxytetracycline treatment was started before admission. All patients received saline transfusions and other measures. *Vibrio cholerae* was isolated from the stools of 272 patients, 190 of whom were given oxytetracycline. Of these 190 patients, 46 received the drug within 6 hours of onset of the disease and 63 between 6 and 12 hours of onset, 2 of the former and 13 of the latter dying. Of the 82 control patients, 12 received other treatment within 6 hours and 20 between 6 and 12 hours of onset respectively, one of the former and 6 of the latter dying. Thus the mortality was much lower among the earlier treated cases of both groups, and oxytetracycline had no apparent influence. Similarly in both groups the mortality was much higher among patients whose systolic blood pressure was below 50 mm. Hg, and oxytetracycline had no apparent effect in such cases. The vibriocidal action of oxytetracycline was shown by the more rapid disappearance of the organism from the stools in treated cases, but the drug did not appear in the faeces in sufficient concentration to have a bactericidal effect on staphylococci until 6 or more hours after its administration.

The authors conclude that oxytetracycline, given orally, has no significant influence on the clinical course of cholera; they noticed, however, that in treated patients formed stools appeared somewhat earlier than in the controls. *J. F. Corson*

1561. **Intravenous Terramycin in Cholera**
A. Das, S. Ghosal, and S. K. Gupta. *Journal of the Indian Medical Association* [*J. Indian med. Ass.*] **22**, 272–273, April, 1953. 2 refs.

As fluid passes so quickly from the blood into the bowel in cholera, it was hoped that oxytetracycline injected intravenously would reach the intestine in effective amounts more rapidly than when given by the mouth. At the Nilratan Sarkar Hospital, Calcutta, a single dose of 500 mg. of the drug was added to the first pint (568 ml.) of intravenously administered saline solution in 20 unselected cases of cholera in which vibrios were demonstrable, 16 orally-treated cases serving as controls.

None of the treated patients died, and only 2 of the controls, a statistically insignificant difference. However, in only 3 of the 20 treated cases were vibrios present on the 2nd day and in none during the next 4 days, whereas among the controls vibrios were present in 12 cases on the 2nd day, in 11 on the 3rd day, and in 4, 2, 1, and *nil* respectively on the four subsequent days, suggesting that the drug appears more rapidly in the stools when given intravenously than by mouth. Cultures of samples of faeces taken 2 and 6 hours after injection of the drug showed no marked reduction in the number of colonies grown, although 6 of 10 samples at 6 hours contained the drug in concentrations of 4 to 16 μg. per ml., the vibriostatic concentration *in vitro* being 2 to 5 μg. per ml. *J. F. Corson*

1562. **Antibiotics in Acute Bacillary Dysentery. Observations in 1,408 Cases with Positive Cultures**
B. T. Garfinkel, G. M. Martin, J. Watt, F. J. Payne, R. P. Mason, and A. V. Hardy. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **151**, 1157–1159, April 4, 1953. 8 refs.

Bacillary dysentery is a disease which occurs in epidemic form among confined populations. Despite attempts at prevention, outbreaks occurred in prisoner-of-war camps in Korea. Treatment was complicated by the fact that nearly all the pathogenic organisms responsible for these outbreaks were resistant to the sulphonamides. The authors report the results of treatment with certain antibiotics, their analysis being based only on cases (to a total of 1,408) in which the diagnosis had been confirmed both bacteriologically and sigmoidoscopically. [The exact types of *Shigella* are not specified, but all the cases are said to have been severe.] The duration of symptoms before the patient's admission to hospital was usually 4 to 6 days. Different groups were treated with sulphadiazine, polymyxin B, chloramphenicol, aureomycin, and oxytetracycline (" terramycin "). The percentage of positive stool cultures at various intervals was used to assess therapeutic efficacy.

The results in patients treated with sulphadiazine were not significantly different from those in a group treated by supportive methods only: the number of patients with a positive culture fell gradually until the end of a week, when about a quarter of the total still gave positive findings. Slightly better results followed treatment with polymyxin B, which was given in doses of 50 mg. twice a day for 7 days or in doses of 100 mg. 4 times a day for 5 days.

With the other antibiotics much better results were obtained, cultures in most cases becoming negative in 2 days and remaining so. A dose of 4 g. of aureomycin,

oxytetracycline, or chloramphenicol given during 24 hours was as effective as the larger doses commonly employed. [No mention is made of toxic effects or of the occurrence of relapses.]

Results of follow-up sigmoidoscopic examination, records of the daily frequency of stools, and the physician's notes on the patients' clinical condition were also used as indices of the response to treatment. [Although it is stated that " these observations paralleled the findings reported above ", no details are given.]

H. David Friedberg

1563. **Chloroquine in the Treatment of Amoebic Liver Abscess**

J. C. PATEL. *British Medical Journal* [*Brit. med. J.*] **1**, 811–813, April 11, 1953. 8 refs.

After reviewing the literature on the use of chloroquine in protozoal infections, the author describes the results of treatment with this drug in 11 cases of amoebic liver abscess at the King Edward Memorial Hospital, Bombay, in all of which the diagnosis was established by aspiration of characteristic pus. The drug was given orally in a dose of 0·25 g. twice daily. In the first 6 cases treatment was given for 10 to 12 days, but as the condition relapsed in 2 patients the duration of treatment was extended to 30 days. There was no relapse in the other 9 patients. One death occurred in the series, in a patient in relapse; otherwise, the treatment was successful. Only minor toxicity was observed; in this respect the drug compares favourably with emetine. The author suggests that further work is required to determine the dosage of the drug and the duration of treatment necessary in cases of amoebic liver abscess.

J. L. Markson

1564. **Fumagillin as an Amebacide. Preliminary Report**

G. MCHARDY, J. E. BECHTOLD, G. E. WELCH, and D. C. BROWNE. *Southern Medical Journal* [*Sth. med. J. (Bgham, Ala.)*] **46**, 428–433, May, 1953. 15 refs.

The efficacy of fumagillin, a substance isolated from *Aspergillus fumigatus* and previously shown to be a highly effective direct-acting amoebicide *in vitro* and *in vivo*, was investigated at Touro Infirmary, New Orleans. Tolerance tests were first carried out on 10 volunteers, the dosage being 10 mg. a day, increased by daily increments of 10 mg. to a maximum of 100 mg. daily. Anorexia occurred in all 10 subjects with a dose of 30 mg., while nausea and abdominal discomfort were consistently complained of when the daily dose was 60 mg. Vomiting occurred in one case after a 90-mg. dose, mild diarrhoea in 2 with a 70-mg. dose, the diarrhoea subsiding 48 hours after the end of the trial, and mild vertigo in 8 with a dose of 60 mg. or more. No renal, hepatic, or blood changes were observed during or after administration of the drug.

To 64 patients suffering from intestinal amoebiasis, 6 of whom had been treated with other drugs without success, fumagillin was given in a dosage of 20 mg. three times a day for 10 days. The diagnosis was based on identification of *Entamoeba histolytica* cysts or trophozoites in the stool, and the criteria for cure were negative stools and, in cases with ulceration initially, evidence of healing of the ulcer on procto-sigmoidoscopy and radiological examination. Side-effects were transient, mild, and relatively infrequent, and in no case caused interruption of treatment. As in the 10 volunteers, no renal, hepatic, or blood changes were seen. Of the 64 patients, 12 had acute amoebic ulcerative colitis, 18 chronic amoebic ulcerative colitis, while 34 were asymptomatic. The follow-up period was 8 months in 18 cases, 6 months in 22, and 4 months in 24. The condition recurred in 2 patients within three months and in one, in whom reinfection was suspected, after 6 months.

Other organisms present initially which were also eradicated were: *Trichomonas* in 8 cases, *Trichocephalus* in 5 cases, and *Giardia* in 4 cases. *Ascaris* (present in 6 cases) and *Strongyloides* (3 cases) were not influenced to any degree. Species of *Entamoeba* other than *E. hystolytica* were eradicated from 7 out of 12 cases.

I. M. Rollo

1565. **Observations on the Treatment of Amoebiasis with Terramycin and Fumagillin.** (Observations sur le traitement de l'amibiase par la terramycine et la fumagilline)

G. C. THOORIS and J. F. KESSEL. *Presse médicale* [*Presse méd.*] **61**, 705–706, May 16, 1953. 12 refs.

In an investigation of the prevalence of intestinal parasitism in Tahiti, 692 individuals were examined, of whom 22·3% were found to be passing either vegetative forms or cysts of *Entamoeba histolytica*.

Of these, 38 persons with intestinal amoebiasis, ranging in age from 5 to 76 years, were selected for treatment with oxytetracycline (" terramycin "). The dosage employed was as follows: for adults, 8 capsules (each of 250 mg. of the hydrochloride) per day for 3 days, then 10 capsules per day for 7 days; for children, 4 to 8 capsules a day for 10 days, each daily dose being about 40 mg. per kg. body weight. The side-effects included diarrhoea and nausea, but were in no case sufficiently severe to interrupt treatment.

The results [judged on what was, perhaps, a slightly inadequate test of cure] were excellent. In all the cases there was clinical improvement, and the faeces were negative for amoebae and cysts at the end of treatment; at the end of 6 months, in 28 (87%) of 32 cases examined, the faeces were still negative. The effect of the drug on other parasites was also studied, and it appeared to be effective (though not completely so) against other protozoa such as *Proteus morgani*, against *Shigella*, and possibly against *Treponema*.

Fumagillin was used in treating 12 patients aged 4 to 56 years. The adults were given one 10-mg. capsule 3 times a day for 3 days, then 2 capsules 3 times a day for 12 days; children received a proportionate dose. Vomiting and diarrhoea occurred in one case, and hepatic pain in another. At the end of treatment there was clinical improvement in 11 cases, and the stools of 10 were negative; after 3 months no further cases with positive stools were found. Fumagillin also appeared to be active against certain other intestinal parasites.

The authors conclude that both these substances are active amoebicides, but that a further study of the efficacy of fumagillin is necessary.

W. H. Horner Andrews

Allergy

1566. **The Incidence of Respiratory Allergy as Disclosed n a Survey of 37,497 Persons, 1949–1950**
W. B. Blanton, E. C. Matthews, M. T. Tobin, and S. E. Shanks. *Industrial Medicine and Surgery* [*Industr. Med. Surg.*] **22**, 99–102, March, 1953. 16 refs.

From December, 1949, to August, 1950, 37,497 individuals over the age of 15 in Richmond, Virginia, were questioned and appropriate tests applied for evidence of 11 chronic diseases—asthma, seasonal hay-fever, perennial hay-fever, anaemia, syphilis, diabetes, heart disease, hypertension, hypotension, rheumatic fever, and tuberculosis. The results showed an incidence of asthma of 2·6%, of seasonal hay-fever of 3·0%, and of perennial hay-fever of 1·1%, and an over-all incidence of respiratory allergic affections of 6·0%. There was no marked sex differentiation, though there was a higher incidence in white than in non-white persons. In spite of reports that asthmatic subjects do not develop diabetes and that tuberculosis rarely or never coexists with asthma, the present survey showed, among other things, that those with asthma had a higher incidence of hypertension, diabetes, and tuberculosis than normal, though they were less likely to have anaemia or heart disease.

A. W. Frankland

1567. **Summer Hay-fever and Asthma Treated with Antihistaminic Drugs**
A. W. Frankland and R. H. Gorrill. *British Medical Journal* [*Brit. med. J.*] **1**, 761–764, April 4, 1953. 10 refs.

This investigation, carried out at St. Mary's Hospital, London, was designed to test the efficacy in hay-fever and summer asthma of a new antihistaminic drug, and also to determine whether there was any difference in the incidence of asthma between treated and untreated cases of hay-fever.

The patients were divided into three groups of about 50 each, the groups being comparable in regard to age and sex. The first group were treated with 100-mg. tablets of mepyramine maleate (" anthisan "), the second with 10-mg. tablets of the new antihistaminic preparation, 3-pyrrolidino-1-(4′colophenyl)-1-(2′pyridyl) prop-1-ene maleate (" 405-c-49 "), and the third, a control group, were given inert tablets of lactose, care being taken that neither the doctor nor the patient knew which of the three forms of treatment was being prescribed.

A preliminary dosage of 4 tablets a day was suggested, and only patients with seasonal rhinorrhoea, with or without asthma, were accepted for treatment. Each patient was asked to keep a daily record stating the number of tablets taken and whether these produced good, moderate, or poor relief. In assessing results, if the number of " good " days exceeded the total number of " moderate " and " poor " together, the result was classed as " good "; similarly, if the number of " poor " days exceeded the number of " moderate " and " good ", the result was called " poor ". The results, which are tabulated, showed that the new antihistaminic drug 405-c-49 compared favourably with mepyramine maleate. The proportion of patients who developed asthma for the first time during the trial period was the same in each of the three groups, and there was no other evidence to show that the use of antihistaminic drugs predisposes to the development of asthma in hay-fever subjects. The result of treatment with antihistaminics was considerably better in those patients who did not have asthma than in those with asthma.

R. S. Bruce Pearson

1568. **The Effect of Prolonged Administration of Epinephrine on Adrenal Cortical Function and Epinephrine Tolerance in Chronic Asthmatics**
A. Leslie, W. H. Blahd, and W. S. Adams. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **41**, 865–870, June, 1953. 3 figs., 17 refs.

At the University of California Medical Center the opportunity was taken to investigate the effect of prolonged administration of adrenaline in 5 male patients who had been taking adrenaline regularly by subcutaneous injection for considerable periods for asthma, the object being to determine whether there was any evidence of sustained adrenal stimulation of the hypothalamus–adrenal–pituitary system, or if after a time this system became refractory. In addition, by giving regular doses of adrenaline for periods of one week interrupted by one week's treatment with pethidine (" demerol "), the question of adrenaline resistance and the possible restoration of sensitivity after deprivation was also studied. Lastly, the changes in the eosinophil count and in the sweat sodium content were studied during the administration of ACTH and compared with these values when adrenaline alone was given.

The authors found no evidence that adrenaline produced any long-standing stimulation of the pituitary–adrenal axis, or of any increased sensitivity to adrenaline after its discontinuation for a week. Even when the response to adrenaline was reduced the administration of ACTH still had a beneficial effect, indicating different modes of action of the two substances. There was not always a close correlation between clinical improvement with ACTH and the degree of eosinopenia or the reduction in the sweat sodium content. *K. Gurling*

1569. **Adrenalone. Chemical and Pharmacological Properties and Application to the Treatment of Asthma and Asthmatic Dyspnoea.** (Adrénalone. Propriétés chimiques et pharmacologiques. Applications au traitement de l'asthme et des dyspnées asthmatiformes)
A. Ravina and P. Maignan. *Thérapie* [*Thérapie*] **8**, 224–230, 1953. 11 refs.

Nutrition and Metabolism

1570. **Studies in the Utilization of Fructose Administered Intravenously in Man**
J. M. BEAL, J. L. SMITH, and P. M. FROST. *Surgery* [*Surgery*] **33**, 721–730, May, 1953. 6 figs., 20 refs.

In view of recent statements that invert sugar and fructose, given intravenously, are better retained and utilized than glucose, a comparative study of the utilization of glucose and fructose was carried out by the authors at the Wadsworth Hospital, Veterans Administration Center, Los Angeles. The subjects were male surgical patients aged 29 to 69 years who were not in the immediate postoperative period or suffering from any debilitating disease, and two series of experiments were carried out. In the first series (11 subjects), after a preliminary control period and a 9-hour fast, the blood levels of sodium, potassium, glucose, and fructose were estimated and a 24-hour urine collection was started. Four of the subjects were then given 1 litre of 10% fructose and the remaining 7 subjects 1 litre of 10% glucose solution in distilled water by the intravenous route over a period of 2½ to 3½ hours. Blood glucose and fructose estimations were made ½, 1, 2, and 3 hours after starting the infusion, and urine was collected after 2, 4, 6, 8, and 24 hours and its content of glucose, fructose, sodium, potassium, and chloride estimated. During the 24-hour period the subject was allowed only 500 ml. of distilled water by mouth. The subjects of the second series of experiments underwent a preliminary 24-hour control period followed by a 9-hour fast, as in the first series. Over a 5-day period, 4 of them then received 3 litres of 10% fructose and 4 the same amount of 10% glucose solution intravenously every 24 hours, with 500 ml. of 0·9% saline and 20 to 60 mEq. of potassium as potassium chloride. Up to 500 ml. of distilled water daily was allowed by mouth. Urine and blood samples were collected at the same intervals as before on the first day, and daily thereafter. [For details of the methods of estimation used the original paper should be consulted.]

The patients in the first series receiving glucose excreted an average of 3·57 g. of reducing sugar in the 24 hours, whereas those who received fructose excreted 6·57 g. Maximum excretion of sugar occurred 4 to 6 hours after starting the infusion, which was 1½ to 2 hours after the blood levels had returned to normal. Increased sodium and potassium excretion was noted in the subjects receiving fructose. In the second series also, those subjects receiving fructose consistently excreted more reducing sugar and electrolytes in each 24-hour period than those given glucose, the urine containing significant quantities of fructose. The authors therefore conclude that fructose is less well retained and utilized than glucose when given intravenously, and in addition has a diuretic effect, with increased loss of electrolytes. They discuss the possible reasons for the differences between their results and those of previous observers.

R. St. J. Buxton

1571. **A Comparison of the Metabolism of Fructose and Glucose in Hepatic Disease and Diabetes Mellitus**
L. H. SMITH, R. H. ETTINGER, and D. SELIGSON. *Journal of Clinical Investigation* [*J. clin. Invest.*] **32**, 273–282, April, 1953. 6 figs., 35 refs.

At the Walter Reed Army Hospital, Washington, D.C., the authors made observations on the utilization of fructose in the normal subject compared with that in the diabetic and in patients with cirrhosis or hepatitis. They also compared the metabolism of fructose with that of glucose in the same groups. The sugars were administered by continuous intravenous infusion. It was shown that whereas glucose tolerance in patients with diabetes and with hepatic disease was grossly abnormal, fructose tolerance in these subjects was almost normal. Moreover, it was shown in a normal subject that the addition of insulin at a rate of 0·4 unit per minute to a constant infusion of fructose had no effect on the blood fructose level, although that of glucose fell markedly. A fall in serum inorganic-phosphate level was noted during the infusion of each sugar in all three groups, the fall being much more marked during the administration of fructose than of glucose. The blood lactic acid level underwent a slight increase in normal subjects and in patients with hepatitis during glucose infusion, but fell in the diabetic and cirrhotic patients; when fructose was given, however, there was a marked increase in all groups. An increase in blood pyruvate level was noticed in all patients during the infusion of both sugars, but was considerably greater with fructose. It is interesting to note that the maximum serum levels of lactic acid, pyruvate, and α-ketoglutaric acid occurred during the time that the phosphate level was at its lowest.

The authors conclude from the fact that the depression of the serum phosphate level and increase in that of intermediate metabolites was greater when fructose was given that the metabolic pathways for the two sugars are different.

J. N. Harris-Jones

1572. **Some Apparent Anomalies of Potassium Metabolism**
I. W. MACPHEE. *British Medical Journal* [*Brit. med. J.*] **2**, 528–531, Sept. 5, 1953. 1 fig., bibliography.

1573. **Sodium as a Toxic Ion in Potassium Deficiency**
P. R. CANNON, L. E. FRAZIER, and R. H. HUGHES. *Metabolism* [*Metabolism*] **2**, 297–312, July, 1953. 12 figs., 42 refs.

1574. **Familial Primary Amyloidosis with Nervous System Involvement**
A. D. KANTARGIAN and R. N. DEJONG. *Neurology* [*Neurology*] **3**, 399–409, June, 1953. 6 figs., 20 refs.

1575. **Volvulus of the Colon: a Complication of Sprue**
I. GLAZER and D. ADLERSBERG. *Gastroenterology* [*Gastroenterology*] **24**, 159–172, June, 1953. 17 refs.

Gastroenterology

1576. **Bucco-pharyngeal Ulcerations of Undetermined Aetiology**
K. HARRISON. *Journal of Laryngology and Otology* [*J. Laryng.*] **67**, 197–202, April, 1953. 6 figs., 10 refs.

In this paper is reported a clinical study of 7 cases of recurrent ulceration of the mouth and pharynx in adults. Bacteriological examination, virus culture, Wassermann test, complement-fixation test for herpes simplex, biopsy, fractional test meal, radiological examination of chest, and skin tests threw no light on the condition. It was found that a paint consisting of 0·25 g. of aureomycin in 50 ml. of glycerin relieved the pain in 24 to 48 hours, the ulcers healing in about 2 weeks. Recurrence was, however, not prevented, and the patients were taught to paint the ulcers for themselves. *X*-ray therapy in small doses of 100 r weekly for 10 weeks was given in 2 cases. The ulcers healed during the treatment, and so far (one year and 4 years after treatment respectively) there has been no recurrence. Treatment with cortisone was found to be of no value. *S. A. Beards*

1577. **Prosthetic Mucosal Hypertrophy in the Mouth, Simulating Malignancy**
J. WALTER. *British Medical Journal* [*Brit. med. J.*] **1**, 1429–1431, June 27, 1953. 2 figs., 12 refs.

OESOPHAGUS

1578. **The Emergency and Definitive Treatment of Bleeding Esophageal Varices**
R. R. LINTON. *Gastroenterology* [*Gastroenterology*] **24**, 1–9, May, 1953. 5 refs.

At the Massachusetts General Hospital, Boston, before 1945, 76% of patients with Banti's disease and cirrhosis of the liver treated for oesophageal bleeding died, 47% of these as a direct result of haemorrhage. Since 1945, of 99 cases of hepatic cirrhosis, 33 have been treated by a shunting operation; but it is significant that of the remaining 66, 32 died of bleeding or of hepatic failure precipitated by bleeding from oesophageal varices before surgery could be undertaken.

In the emergency treatment of bleeding oesophageal varices the author recommends first the application of pressure to the varices by an intragastric balloon. He has found that a single balloon, introduced into the stomach and kept in firm contact with the cardia by traction with a 2-lb. (1-kg.) weight, is as satisfactory as an intra-oesophageal balloon. After bleeding has been controlled, direct surgical attack is then made on the varices by longitudinal incision of the oesophagus and suture of the three groups of varices at their lower end as recommended by Boerma (*Arch. chir. neerl.*, 1949, **1**, 4174) and by Crile (*Arch. Surg.* (*Chicago*), 1950, **61**, 654; *Abstracts of World Surgery*, 1951, **9**, 235), although the present author prefers to make an incision through the cardia itself which is sutured transversely. [This may lead to peptic oesophagitis; Crile's technique of a simple incision 5 cm. above the cardia is safer. (See Abstract 1580).] In 14 cases so treated only one patient died, but in 5 cases haemorrhage occurred again between 2 weeks and 5 months later.

For this reason a shunting operation is recommended in suitable cases 3 or 4 weeks after suture, when the protein reserves and blood volume are restored. As there is no evidence that a shunting operation improves liver function it is not indicated for ascites, and haemorrhage from oesophageal varices is the only indication. Between 1945 and 1951 79 shunting operations have been performed—25 for extrahepatic and 54 for intrahepatic block causing portal hypertension. Of these patients, 12 died, 7 of haemorrhage, 4 of liver failure, and one of sepsis. Among the 67 survivors (including 52 treated by spleno-renal anastomosis) there have since been 4 cases of minor and 6 cases of major oesophageal bleeding.
Norman C. Tanner

1579. **Effects of Surgical Treatment of Esophageal Varices on the Portal Venous Pressure and Hepatic Function: Preliminary Observations**
E. D. PALMER, V. M. SBOROV, and E. J. JAHNKE. *Gastroenterology* [*Gastroenterology*] **24**, 10–15, May 1953. 2 figs., 3 refs.

In the treatment of oesophageal varices shunting operations to reduce the portal venous pressure have become reasonably safe, but have not yet been proved to be effective in preventing further bleeding from the varices. In an endeavour to judge the effectiveness of these shunts, the authors, working at the Walter Reed Army Hospital, Washington, D.C., determined the pressure in the varices in 9 patients before and after operation by a transoesophagoscopic needle-puncture technique which they consider to be reasonably accurate. In some of the cases the varices had disappeared after operation, so that postoperative pressure could not be determined.

In one patient, in whom the hepatic and splenic arteries were ligated, the pressure in the varices had returned to the preoperative level by the 4th month. Of 3 patients undergoing spleno-renal anastomosis, in 2 no varices were seen at the 5th month, while in the third the varices were small and the pressure normal at the 6th month, but 1½ years later the pressure was higher than before operation. In the only patient treated by side-to-side porta-caval shunt the varices diminished postoperatively but had developed again by the 19th month, while in 3 other patients examined 4 to 6 months after end-to-side porta-caval anastomosis the varices had disappeared.

In all these operations there was a gratifying fall of pressure in the portal vein during the operation, and no

evidence of diminished liver function was observed subsequently. In all cases there was a great diminution in the amount of oesophageal bleeding after the shunting operation, and no bleeding at all after the end-to-side porta-caval shunt. *Norman C. Tanner*

1580. **Treatment of Esophageal Varices by Transesophageal Obliteration**

G. CRILE. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **96**, 573–576, May, 1953. 1 fig., 1 ref.

The author reports, from the Cleveland Clinic, Ohio, the results of treatment of oesophageal varices by transoesophageal obliteration in 9 children and young adults with Banti's syndrome. Of these patients, 7 were the subject of a preliminary report (*Arch. Surg.* (*Chicago*), 1950, **61**, 654; *Abstracts of World Surgery*, 1951, **9**, 235) and have now been followed up for 33 to 48 months after operation, the other 2 having been operated upon since the previous report was published. As in all 9 of the patients the liver was normal and in 6 of them there was no evidence of portal hypertension, it was assumed that the block was limited to the splenic vein. Splenectomy had already been performed in these cases, but it is pointed out that where varices are large or of long standing their walls are thin and there are easily visible anastomotic channels connecting them to the azygos veins. These veins being without valves, the varices continue to fill after their portal supply has been cut off and are therefore still liable to bleed if subjected to trauma. For this reason the author is of the opinion that operations designed to lower the portal venous pressure have little application in cases of extrahepatic block, and for such cases he has introduced the operation of transoesophageal ligation of the oesophageal varices. He makes a 1-in. (2·5-cm.) longitudinal incision in the oesophagus about 2 in. (5 cm.) above its lower end, and obliterates with a running suture each of the three large varices which present, and which closely resemble haemorrhoids.

Of the 7 cases previously reported, haemorrhage has occurred during the follow-up period in only 2; one of these patients, who has had 312 transfusions of blood in the past 7 years, had 2 small haemorrhages just after the operation but has had none since, the bleeding in the other case being ascribed to a gastric ulcer.

H. Daintree Johnson

1581. **The Diagnosis of Cardiospasm**

A. M. OLSEN, C. B. HOLMAN, and H. A. ANDERSEN. *Diseases of the Chest* [*Dis. Chest*] **23**, 477–497, May, 1953. 7 figs., 31 refs.

The authors discuss the diagnosis of cardiospasm on the basis of a study of the records of 601 patients first seen at the Mayo Clinic during the 12-year period 1935–46. After defining the condition and briefly referring to the literature, they analyse the sex and age incidence and other findings in the cases reviewed.

According to the authors radiological examination with barium swallow is the most important diagnostic procedure, and they discuss this aspect at some length. They state that cardiospasm may be divided into four stages: in Stages 1 and 2 excessive muscular activity may be seen, and in Stages 3 and 4 there is atonia with progressive dilatation and kinking of the oesophagus. Diagnosis may be difficult in the early stages. Tertiary contractions are sometimes seen in Stage 1 and following treatment. Some examples of the appearances seen radiologically are illustrated.

The differential diagnosis is fully discussed. The authors consider that the passage of bougies is of value diagnostically as well as therapeutically; for example, the firm resistance encountered when a neoplasm is present is in marked contrast to the sensation experienced by the operator in cases of cardiospasm. In their opinion oesophagoscopy is of limited value.

The incidence of associated diseases is not thought to be high, but such conditions should not be overlooked. The occasional occurrence of cardiospasm in children should be borne in mind.

[This is a well-written article and a useful contribution to the subject.] *Sydney J. Hinds*

STOMACH AND DUODENUM

1582. **Gastritis and Gastroscopic Biopsy**

S. SELESNICK and E. D. KINSELLA. *New England Journal of Medicine* [*New Engl. J. Med.*] **248**, 842–844, May 14, 1953. 10 refs.

The authors of this paper from Yale University School of Medicine have examined the view expressed by Benedict (*Gastroenterology*, 1948, **11**, 281) that no gastroscopic examination is complete unless biopsy under direct vision is performed. A review of 56 gastroscopic examinations with mucosal biopsy on 50 patients was carried out, in all of which the gastroscopic diagnosis was of " gastritis " or " normal mucosa ". The gastroscopist considered that in 23 out of 56 examinations the mucosa appeared normal, but the pathologist concurred in only 14 cases (60%), evidence of gastritis being found in the remaining 9 specimens (40%). In 33 examinations the gastroscopist found evidence of gastritis and the pathologist concurred in 30 cases (91%). The authors conclude that the gastroscopic recognition of gastritis is usually correct, but an apparently normal mucosa may show histological changes of " gastritis ". Benedict's dictum is confirmed. *I. McLean-Baird*

1583. **Colonic Replacement and Restoration of the Human Stomach**

J. MORONEY. *Annals of the Royal College of Surgeons of England* [*Ann. roy. Coll. Surg. Engl.*] **12**, 328–348, May, 1953. 6 figs., 3 refs.

In view of the unsatisfactory results often following the now classic Billroth operations for gastrectomy, the defects of which are discussed, the author devised a new technique, which he introduced a little over 2 years ago in his work at Broadgreen Hospital, Liverpool. In this a segment of transverse colon is interposed between the gastric stump and the duodenum after gastric resection, this segment replacing the stomach and preventing weight loss, malnutrition often leading to chronic pul-

monary infection, and other post-gastrectomy syndromes, which the author attributes to: (1) the loss of the gastric reservoir; and (2) the loss of gastro-duodenal continuity. The use of a jejunal segment was rejected on the ground that the jejunal mucosa is well known to be liable to ulceration when exposed to gastric juice in the absence of pancreatic juice and bile. The advantages of the colon are: (1) it secretes protective mucus; (2) it is capacious; (3) it can be used antiperistaltically; (4) it has no active part to play in the absorption and digestion of food and is normally slightly acid; and (5) bile can be washed back to the gastric stoma.

The results of the first 150 operations are reported, the cases concerned comprising 82 cases of duodenal ulcer, 27 of gastric ulcer, 11 of duodenal and gastric ulcers combined, 10 of recurrent ulcer, and 20 colonic replacements for postgastrectomy syndromes. There were 5 postoperative deaths, 2 of which were due to leaks or abscesses (which also occurred in 3 other cases). At follow-up examination 18 results were considered to be unsatisfactory, including 3 proven cases of recurrent ulcer, 5 other cases of dyspepsia with hyperchlorhydria, and one case of haemorrhage. Most of these were thought to have resulted from inadequate resection early in the series. There were also 3 cases of colo-duodenal stricture, 1 of duodenal ileus, and 5 cases of coincidental disease.

Occasional early postoperative sequelae are epigastric fullness and aching in the left hypochondrium, windy discomfort and " enjoyment of breakfast more than the evening meal ". In some cases tea may cause a choking sensation. Food capacity has varied enormously in different patients, but the author considers a three-quarters gastrectomy with a 5-inch (12·5-cm.) loop of colon, which has given an emptying time of about 1 hour, to be about right. Of the first 100 patients, 19 have fully recovered and in 62 the body weight is now above the preoperative level. In 5 patients with carcinoma colonic replacement was carried out after total gastrectomy; of the 3 survivors of this procedure, 2 are now above their preoperative weight and the third is very near to it.

[This paper records another important and original contribution in the modern era of surgery with replacement. The three remarkable results after total gastrectomy for cancer are specially to be noted. Anyone interested in this operation would do well to read the original paper.] *H. Daintree Johnson*

1584. **Gastric Block. A Disturbance of Gastric Motive Function.** [In English]
B. LILJA. *Acta radiologica* [*Acta radiol. (Stockh.)*] **39**, 353–367, May, 1953. 21 figs., 4 refs.

In the period 1946–51, 22 patients at the Central Hospital, Halmstad, Sweden, were subjected to gastrectomy for ulcer at, or just above, the incisura angularis of the lesser curve of the stomach. In 18 cases the proximal part of the pyloric antrum, that is, the lowest part of the greater curve, was dilated (characteristic radiographs are reproduced). In the 4 cases with no dilatation the ulcer crater " appeared to be somewhat smaller ". [The histology here is less convincing, but possibly the destruction of the muscular wall by the base of the ulcer was less complete.]

The author puts forward the following theory. Embryologically, the stomach is an asymmetrical dilatation to the left of the primitive digestive tube. The vertical part of the stomach, as far as the angulus, belongs to the oesophagus, while the transverse part, with the pyloric glands, belongs to the intestine. Both in the cat and in man peristaltic waves are often two or three times as frequent in the vertical part of the stomach as in the horizontal. It is possible, therefore, that the peristaltic wave passing down the vertical part of the stomach excites the pacemaker at the angulus. If this pacemaker is destroyed by an ulcer, or experimentally by a wedge excision, peristalsis and gastric emptying will be disturbed and the characteristic change in the appearance of the stomach will result. The practical importance of this disturbance in function is that it is an indication for surgery. The word " block " is borrowed from cardiac pathology in the hope that it will make the clinicians pay more attention to the problem of gastric emptying.

[It has long been recognized that shortening of the lesser curve of the stomach is associated with delayed emptying. The extreme case of this is the " hanging-bag " deformity, where the pylorus opens vertically upwards and surgery is essential; the operation of wedge excision of a gastric ulcer was given up because it tended to produce this deformity and even if there was no recurrence of the ulcer, the patient complained of a feeling of distension and of acid regurgitating into the mouth. Stomach contractions and pyloric relaxation were not coordinated, the wave of peristalsis reaching the pylorus too soon along the lesser curve, and too late along the greater curve. Thus the pylorus failed to relax at the height of the gastric contraction and hence acid and food tended to be driven back into the oesophagus. This paper will have served a useful purpose if it stimulates interest in how the stomach empties.] *Denys Jennings*

1585. **Antrum Motility as a Stimulus for Gastric Secretion**
L. R. DRAGSTEDT, H. A. OBERHELMAN, J. M. ZUBIRAN, and E. R. WOODWARD. *Gastroenterology* [*Gastroenterology*] **24**, 71–78, May, 1953. 3 figs., 8 refs.

A series of operations on the stomach of a dog were carried out at the University of Chicago in order to study the nervous and hormonal factors stimulating gastric secretion. The complicated operative procedures are enumerated below; in each case the amounts of secretion mentioned refer to the gastric pouch and were the results of 24-hour collections, the figures being the average of those made over the course of several weeks.

(1) A Pavlov pouch was formed, leaving the vagal innervation intact; the average daily secretion of gastric juice was 1,000 ml., containing 150 mEq. of free hydrochloric acid. (2) The pyloric antrum was resected and marsupialized to the anterior abdominal wall, alimentary continuity being re-established by anastomosing the

proximal end of the resected stomach to the duodenum; the secretion was then 425 ml., with 50 mEq. of acid. (3) The Pavlov pouch was transformed into a Heidenhain pouch by separating it completely from the body of the stomach, thus destroying its vagal innervation; this resulted in a secretion of 150 ml., containing 15 mEq. of acid. (4) The pyloric antrum was removed from the anterior abdominal wall and implanted into the colon; 800 ml. of juice containing 120 mEq. of acid were then produced. (5) Two-thirds of the antrum was excised, and all vascular and other connexions with its original bed severed; the amount of secretion then fell to 225 ml., with 30 mEq. of acid. (6) The segment of colon containing the antral implant was dissociated from continuity with the alimentary tract, the distal end closed, and the proximal end exteriorized; secretion now rose to 550 ml., with 75 mEq. of acid. Finally, (7) the distal end of the colonic segment was also exteriorized; this caused a fall in secretion to 100 ml., containing 10 mEq. of acid, but when the distal end of the segment was obstructed, secretion immediately rose again to 550 ml. with 70 mEq. of acid.

These procedures were repeated in an unspecified number of dogs, and gave comparable results. Defunctioning of the pyloric antrum reduced gastric secretion by two-thirds: resection of the vagi caused another fall of approximately two-thirds. When the isolated colonic segment containing the antrum was obstructed and pressure developed in it by peristalsis, gastric secretion was high: when the obstruction was removed secretion fell by 80%. The authors claim that these results show that the stimulus to antral hormone production is distension of the pyloric antrum.

A. G. Parks

1586. **Late Effects of Antrum Resection on Gastric Secretion**

E. R. Woodward and L. R. Dragstedt. *American Journal of Physiology* [*Amer. J. Physiol.*] **173**, 89–90, April, 1953. 2 refs.

In 1948 the authors, with Bigelow, reported a series of experiments carried out at the University of Chicago in which the gastric acid secretion of 11 dogs with Pavlov or Heidenhain pouches was shown to be greatly diminished following resection of the pyloric antrum. In the present paper they describe a follow-up study of 5 of the dogs which survived for varying periods of time. In one animal which survived for 5 years the total acid secretion remained constant at about 6% of the preoperative level. Another animal showed a marked diminution in secretion for 18 months, but after 2 years the total acid production of the pouch had returned nearly to preoperative levels. In 3 dogs which survived for 6 months there was consistently low acid secretion, varying from 2 to 18% of the amount secreted before antral resection. The responses of the gastric pouches to histamine injection did not vary during the course of the experiment, nor did the dogs deteriorate in general condition. The authors conclude that resection of the pyloric antrum permanently abolishes the gastric phase of gastric secretion. *A. G. Parks*

1587. **A Relationship between Cancer of Stomach and the ABO Blood Groups**

I. Aird and H. H. Bentall. *British Medical Journal* [*Brit. med. J.*] **1**, 799–801, April 11, 1953. 10 refs.

The standardized mortality from cancer of the stomach was shown by Stocks (*Brit. J. Cancer*, 1950, **4**, 147) to be greater in northern than in southern towns in England. It is also known that blood of Group A is found less frequently and of Group O more frequently in the north of England than in the south. In order to test whether these observations are correlated, a survey was made of the ABO distribution in 3,632 proved cases of carcinoma of the stomach in the records of hospitals in Scotland, Newcastle, Leeds, Manchester, Liverpool, Birmingham, and London. For Scotland (478 cases) and the northern towns of England (1,406 cases), the ABO distribution was determined in an equal number of control subjects selected at random from the same hospitals, with two exceptions (556 cases) in which the frequency was derived from the records of the local blood transfusion centre. In the London area (1,340 cases) the figures for controls were those reported by Discombe and Meyer (*Amer. J. Clin. Path.*, 1952, **22**, 543; *Abstracts of World Medicine*, 1952, **12**, 486) for north-west London.

In a statistical analysis of the results (made by Fraser Roberts) the calculation of the ratio of Group A to Groups A+O showed that, irrespective of locality, the incidence of A was significantly greater and of O significantly smaller ($P < 0.0001$) in patients with carcinoma than in the controls. It follows, therefore, that this correlation is not responsible for the known difference in the geographical distribution of cancer of the stomach in England. The authors consider that their findings show that, in the development of cancer of the stomach, there are two factors concerned, an inherited factor related to the ABO system, and another, presumably environmental, factor which is responsible for the greater incidence in the north. They suggest that blood of Group A has a negative selective value and of Group O a positive one. These effects are slight, as the incidence of cancer of the stomach is highest after the age of puberty.

Some interesting comparative figures are quoted from Swiss sources. *M. Lubran*

1588. **Carcinoma of the Stomach. Necessity for Re-evaluation of Therapeutic Philosophy**

A. Ochsner and J. Blalock. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **151**, 1377–1384, April 18, 1953. 7 figs.

In view of the poor degree of operability and the low 5-year survival rate in cases of gastric carcinoma the authors, writing from the Tulane University of Louisiana School of Medicine, New Orleans, propose changes in what they call the "therapeutic philosophy" of this disease.

In about one-third to one-half of cases in which resection of the stomach is performed recurrence of the carcinoma occurs in or near the gastric stump, and involvement of the duodenal stump is reported in between 7 and 70% of cases, though the tumour rarely extends

more than 1 cm. into the stump. The authors have noticed that very small amounts of stomach are often removed for cancer even when the operation is described as " subtotal ". They make a plea for a higher gastrectomy in carcinoma of the stomach, combined with radical resection of the adjacent omenta and lymph nodes, which they believe will give as good results as total resection when dealing with carcinoma of the pyloric end of the stomach.

In this paper they report on 220 cases of primary gastric malignant disease observed in the 10 years ending in January, 1952 (210 of carcinoma, 5 of leiomyosarcoma, 3 of reticulum-cell sarcoma, and one each of lymphosarcoma and Hodgkin's disease). The results are summarized as follows (the percentage in each case being based on the total number of patients). Exploration was performed in 76·6% and resection in 33·3%; 29% survived the resection and 9·9% were alive at the end of 5 years. The hospital mortality rate, according to the type of procedure, was: oesophago-gastrectomy, 50%; total gastrectomy, 30%; exploration only, 13·4%; subtotal resection—curative 9·5%, palliative 7·9%. It was also found that subtotal resection gave a slightly better 5-year survival rate than total resection, thus indicating that radical subtotal gastrectomy gives results (47% of 5-year survivals in this series) as good as any reported by the protagonists of total resection for all cases of gastric carcinoma.

The authors advocate surgery in all cases of gastric ulcer because of the difficulty of differentiating benign from malignant lesions, adding that gastric polyps and persistent gastritis should be treated by gastrectomy on the assumption that these are pre-malignant lesions. They reaffirm Edwards's suggestion that if a patient has clinical evidence of gastric cancer, unsupported by laboratory findings, exploratory laparotomy is imperative. They state that all men past the age of 40, previously well, in whom digestive disturbances develop for the first time and persist require exploratory laparotomy.

Norman C. Tanner

1589. **Inflammatory Fibroid Polyps of the Stomach**
W. K. Bullock and E. T. Moran. *Cancer* [*Cancer (N.Y.)*] 6, 488–493, May, 1953. 12 figs., 3 refs.

1590. **Ulcer of the Greater Gastric Curvature**
A. D. Silk, O. A. Blomquist, and R. Schindler. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **152**, 305–307, May 23, 1953. 3 figs., 4 refs.

Ulcer of the greater curvature of the stomach is a rare condition. The present authors collected a total of 18 cases, 16 of them from the records of the Veterans Administration and White Memorial Hospitals, Los Angeles, and 2 from private practice. Histological examination after operation or at necropsy revealed that the ulceration was benign in 8 of the cases and malignant in 10.

In 3 of the 8 benign cases duodenal ulceration was also found, while in 2 there was ulceration of the lesser curvature of the stomach. In the authors' view the presence of these additional lesions increases the likelihood that the ulceration of the greater curvature is benign. In 3 cases benign ulceration of the greater curvature was associated with primary carcinoma of the lung, and in all 3 cases death was due to haemorrhage from the gastric ulcer.

The authors consider that the mere location of an ulcer on the greater curvature of the stomach should not be taken as indicating malignancy. *D. W. Barritt*

1591. **Prognosis and Treatment in Acute Perforated Peptic Ulcer. A Review of 206 Cases**
J. Gilmour. *Lancet* [*Lancet*] **1**, 870–873, May 2, 1953. 11 refs.

A statistical study is presented of 206 cases of acute perforation of a peptic ulcer, all treated by laparotomy and simple suture at the Royal Victoria Infirmary, Newcastle upon Tyne. These patients were all under the care of a single surgical firm, but were not necessarily operated upon by the same surgeon. The over-all mortality was 6·3%. The cases are analysed with regard to sex, age, site and chronicity of ulcer, and time interval between perforation and operative repair. Acute ulcers accounted for 58% of the perforations, and chronic ulcers for 42% (and all the 13 deaths), the differentiation of an acute from a chronic ulcer being based on the lack of preoperative history of dyspepsia, the mode of onset of the pain, and the findings at operation. On analysis of the late results in these patients it was found that the ultimate prognosis in cases of acute ulcer was, on the whole, good in more than 75%—less than 25% tending to have subsequent dyspeptic symptoms and less than 10% needing further surgery. In contrast, all those with perforation of a chronic ulcer had further symptoms, and a large proportion required further surgery.

The relative merits of simple suture and a more radical resection aimed at permanent cure are discussed, and a tentative plea is made for the latter course in cases of chronic ulcer, provided other factors are favourable.

C. Patrick Sames

1592. **Duodenal Ulcer Treated by Subtotal Gastrectomy with and without Vagotomy. Six-year Comparative Study**
L. J. Druckerman, V. A. Weinstein, P. Klingenstein, and R. Colp. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **151**, 1266–1269, April 11, 1953.

A comparison was made between the results in 220 cases of duodenal ulcer treated by partial gastrectomy (Group 1) and those in 165 cases treated by partial gastrectomy combined with infradiaphragmatic vagotomy (Group 2) at the Mount Sinai Hospital, New York, during the period 1946–51. The average age of the patients in the first group was 48 years and in the second 43·2 years. The postoperative morbidity was slightly higher in Group 2 (combined operation), there being an increased incidence of pulmonary complications and of postoperative distension. There were 2 deaths in the series, both in Group 2, one due to massive pulmonary embolism on the 2nd postoperative day and one due to pancreatic necrosis on the 42nd day. Postoperative

progress during the first 3 months revealed an equal incidence of symptoms of the dumping syndrome. In 4 patients, all in Group 1, there were symptoms of recurrent ulceration, whereas in Group 2 more patients suffered from diarrhoea or vomiting.

Follow-up studies, made at an interval of from 4 months to 6 years after operation, showed that 11 out of 162 patients (7%) in Group 2 had increased bowel movements amounting to diarrhoea (which was disabling in one case), while in Group 1 only 4 patients out of 218 (2%) had slight diarrhoea; and that 10 patients in Group 1 had recurrent jejunal ulceration, whereas there was no case of recurrence in the second group. In Group 1 the results were considered satisfactory in 93% of cases, compared with 98% of those in Group 2. The operation of combined vagotomy and gastrectomy produced gastric anacidity in a notably higher proportion: hence the absence of stomal ulceration in this group.

The authors' general conclusion is that vagotomy is a desirable addition to subtotal gastrectomy in the treatment of duodenal ulcer in cases where it is considered that the operative risk is not materially increased thereby.

Norman C. Tanner

LIVER

1593. **Cortisone in Decompensated Portal Cirrhosis: a Preliminary Report**

S. J. Zoeckler and G. J. Hegstrom. *Gastroenterology* [*Gastroenterology*] **24**, 30–43, May, 1953. 3 figs., 21 refs.

The management of the cirrhotic patient with decompensation is still a difficult problem, and most of the previous reports of the use of ACTH and cortisone in hepatic disease have not been encouraging. In this paper from the Veterans Administration Hospital, Des Moines, Iowa, the authors describe their results in 7 patients suffering from advanced hepatic cirrhosis with ascites who were treated for 21 days with cortisone by mouth, the dosage being 300 mg. the first day, 200 mg. the second, and 100 mg. daily until 14 days had elapsed. The dose was then tapered to conclude with a total amount of 2·025 g. in 21 days. Peritoneoscopy and liver biopsy were carried out on 6 of the 7 patients, and liver function tests were performed before, during, and up to 12 weeks after cessation of the cortisone treatment.

The most significant response noted in all 7 patients was the immediate and striking increase in appetite and a greatly improved sense of well-being, the patients being able to eat a full diet of 4,300 Calories containing 135 g. of protein. All showed increased output of night urine, and fluid retention did not prove a problem. In all cases a rise in the serum albumin level occurred under treatment, and in levels of total cholesterol and cholesterol esters. No toxic effects were observed, and though 2 deaths occurred, in neither case could it be attributed to the cortisone. In all patients the enlarged liver decreased in size, and liver biopsy showed a decrease in fat and in several cases cellular regeneration in previously necrotic liver cells, while in a few cases spider angiomata disappeared during treatment. It seems likely that the main benefits obtained, however, were the reduction of anorexia and lethargy, with corresponding gain in appetite and nutrition, and the authors feel unable to draw a conclusion as to any other more specific effect.

Thomas Hunt

1594. **An Aid in the Diagnosis of Cirrhosis of the Liver.** (Příspěvek k diagnostice jaterních cirrhos)

C. Mastík. *Lékařské Listy* [*Lék. Listy*] **8**, 206–209, May, 1953. 4 figs., 3 refs.

Various changes in the appearance of the nails have been described in association with cirrhosis of the liver. The author studied 49 cases of the disease (41 of which were confirmed at laparotomy) and correlated the changes in the nails with the serum iron level, haemoglobin value, blood protein level, and the results of liver function tests.

Longitudinal grooving of normally formed or flattened nails was the most frequently observed change (26 cases, mainly in older patients). In the majority of these the serum iron level was reduced, but haemoglobin values and liver function tests were inconclusive. The grooving was very marked in 13 cases, and in 11 cases regular and elevated, resembling a string of pearls. Second in frequency, independent of age, was the finding of flattening of the nails (12 cases), either on all fingers, or only on the thumb and second or third finger, associated in some patients with abnormal brittleness. In this group the serum iron and blood protein levels and haemoglobin values showed little deviation from the normal. The liver function tests were slightly raised and the cadmium reactions were positive in 3 patients and greatly raised in 3 others. Test results in the remaining patients were normal. Hour-glass nails, markedly bent in two directions, were found only in 3 patients, but the grooving of the nails in these cases was not marked. Excessive brittleness was observed in 2 cases, in one instance with longitudinal grooving, in the other with flattening.

All the nail changes described were more marked on the fingers than on the toes. The pathogenesis of these changes remains obscure, but it is suggested that disturbances of sulphur metabolism may lead to the abnormal changes in the structure of nails and hair, and that nutritional factors may also have some influence. Hyposideraemia seemed to be related to the grooving of the nails but not to the flattening of them.

M. Dynski-Klein

INTESTINES

1595. **Diverticulosis of the Small Bowel.** (О дивертикулезе тонкого кишечника)

S. A. Dneprovolzhskii. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **31**, 75–78, May, 1953. 3 figs., 3 refs.

The incidence at necropsy of diverticuli in the small intestine, as reported in the [presumably Russian] literature, varies from 3 to 16%; radiologically they are found in 1·2 to 3·7% of cases. The present author

reports 22 cases diagnosed during life among 810 patients investigated for gastro-intestinal disease, an incidence of 2·7%.

In contrast to some previous observations, women predominated (16 cases). Of the 22 patients, 2 had no related symptoms, 12 complained of epigastric pain, nausea, and a heavy feeling after meals, 5 had recurrent diarrhoea, and 7 constipation. The gastric juice was normal in 8, hyperchlorhydric in 6, and hypochlorhydric in 2 cases, while 6 patients were completely achylic. Only 2 patients had multiple diverticula. Of the solitary diverticula, 19 were found in the duodenum, 3 of them in the vicinity of the ampulla of Vater. Six of the patients also suffered from peptic ulcer, and 6 from " duodenitis ". *A. Swan*

1596. **Chronic Ulcerative Granulomatous Jejunitis and Ileojejunitis**
R. H. MARSHAK and B. S. WOLF. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **70**, 93–113, July, 1953. 23 figs., 25 refs.

1597. **Proctalgia Fugax**
M. R. EWING. *British Medical Journal* [*Brit. med. J.*] **1**, 1083–1085, May 16, 1953. 29 refs.

Although Thaysen (1935) is credited with giving the name " proctalgia fugax " to the symptom-complex described in this paper, the author mentions that a short article published by a Dr. Myrtle, of Harrogate, in 1883 shows that the latter was fully aware of the existence of this disorder.

The present paper contains a very clear account of the symptomatology of proctalgia fugax, which is characterized by recurring attacks of deep-seated rectal pain. The condition is considered to have a psychoneurotic origin, proctalgia being the sole somatic manifestation. Treatment is also discussed.

[Although some readers may disagree with the name proctalgia fugax, none will quarrel with this excellent, concise account of an obscure but by no means rare malady.] *C. Patrick Sames*

HERNIA

1598. **Sliding Hernias through the Oesophageal Hiatus**
G. RIOS-SOLANS. *British Medical Journal* [*Brit. med. J.*] **1**, 1029–1030, May 9, 1953. 9 refs.

In describing a study of the aetiology of sliding hernia through the oesophageal hiatus the author points out that, as this type of hiatal hernia is most often encountered in adults past middle age, it should be regarded as distinct from a congenital defect. Considering that knowledge of the exact anatomical status of the so-called " cardia " is essential to such a study, he has examined specimens taken post mortem from 50 unselected adults at the Western Infirmary, Glasgow.

The author observes that where the oesophagus enters the stomach the junction of squamous and columnar epithelium is not circular, but follows an irregular curve, and that this junction corresponds neither with the change from tubular to saccular formation at the cardia nor with the level at which the oesophageal hiatus of the diaphragm embraces the oesophagus. No muscular thickening was found at the lower end of the oesophagus in the specimens examined, and it is the author's opinion that any sphincteric action in this neighbourhood must be weak and probably extending over a segment 1 in. (2·5 cm.) long, rather than being strong and localized as at the pylorus.

Of the 50 specimens examined, the hiatus was found to be patent in 13, the author defining patency as permitting passage of 1 or 2 fingers a distance of 2 to 3 cm. into the mediastinum from the abdominal aspect. Where it was possible to pass the fingers, this was always found to be in the anterior and left lateral aspect and never in the posterior and right lateral aspect. [That is to say, the author could pass his fingers through the hiatus only where the peritoneum lay directly in contact with it. This would not, of course, preclude a hernia *en glissade* in the posterior and right parts of the hiatus.] *H. Daintree Johnson*

1599. **Clinical Picture and Diagnosis of Diaphragmatic Hernia.** (К клинической картине и распознаванию диафрагмальных грыж)
M. N. MYASNIKOVA. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **31**, 45–46, April, 1953.

Diaphragmatic herniae due to trauma (for example, from firearms) are not uncommon and present no great difficulty in diagnosis, but the congenital or non-traumatic acquired types are often recognized only after prolonged and unsuccessful treatment for other conditions.

The case is described of a man of 22 who complained of pains in the retrosternal area and praecordium with radiation to the left shoulder, and of convulsive attacks of 8 months' standing which were accompanied by loss of consciousness and followed by amnesia. Dyspnoea, at first on exertion and later even on walking, was a distressing symptom, but treatment with various medicaments was ineffective. Radiography revealed a shadow in the right pulmonary area which was thought to be a hydatid cyst, but a skin sensitivity test was negative. Electrocardiography showed no changes from the normal. A further radiograph of the chest showed a round swelling, less dense than the lung tissue and not homogeneous, suggesting that it contained gas. A barium-meal examination showed the stomach to be normal, but 24 hours after the meal the hepatic flexure of the colon, filled with barium, was seen to be occupying an area in the right side of the thorax.

A diagnosis of diaphragmatic hernia through the trigonum sternocostale (triangle of Larrey) was made, and the hernia was repaired by a combined transthoracic and abdominal approach. The sac contained transverse colon, stomach, and omentum. After operation the patient's symptoms disappeared entirely.

[It is remarkable that this young man managed to survive 22 years with an apparently congenital pleuroperitoneal hernia without symptoms of any kind until the age of 21.] *L. Firman-Edwards*

Cardiovascular System

1600. **High-frequency Fractionated Systoles and Flutter.** (Les systoles fractionnées à grande fréquence et le flutter) R. LUTEMBACHER. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur*] **46**, 385–392, May, 1953. 2 figs.

In this paper the differential diagnosis by electrocardiography between ventricular flutter and high-frequency fractionated systoles is discussed. The latter is a type of regular paroxysmal ventricular tachycardia in which base and apex of the ventricle contract asynchronously. The supposed pathology is impaired myocardial conduction with the interposition of an ectopic automatic centre emitting impulses at a rate of 250 to 350 per minute; it is not due to a " circus movement ". Experimental production of this condition in the frog and rabbit is described, and electrocardiograms (ECG's) are reproduced. [No account is given of fractionated systoles in man, nor are any tracings from human subjects reproduced.] It is suggested that the crises of ventricular tachycardia recorded in the syncope of Stokes–Adams attacks may be due to fractionated systoles.

The ECG of low-frequency fractionated systoles shows a monopolar, inverted, V-shaped curve due to systole of the base of the ventricle, followed first by a plateau representing a tonic phase and then by a V-shaped curve resulting from the apical systole. As the frequency of the systoles increases, the intervening tonic plateau disappears and there is no T wave, the tracing becoming a regular undulation. To differentiate high-frequency fractionated systoles from flutter, it is necessary to take an ECG with the film moving at high speed. It is then seen that there is a pathognomonic widening or slurring of the peak of the upright wave which might easily be missed on a tracing recorded at the usual rate.

The author concludes by emphasizing that it is important to obtain a rapidly recorded ECG in all cases of apparent flutter in order not to miss the occurrence of fractionated systoles. *D. Goldman*

1601. **The Electrocardiographic Response to the Standard 2-Step Exercise Test**
J. WENER, A. A. SANDBERG, L. SCHERLIS, J. DVORKIN, and A. M. MASTER. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **68**, 368–374, April, 1953. 6 figs., 38 refs.

At the Mount Sinai Hospital, New York City, the changes in the electrocardiogram in response to standard single and double 2-step exercise tests were studied in 311 normal subjects. The number of trips to be taken up and down the steps in 1½ minutes in the single test and in 3 minutes in the double test was determined from a table according to the subject's weight, age, and sex. An electrocardiogram, consisting of leads I, II, III, V4, and V5, was recorded immediately on completion of the test. The double test was carried out only if there were no changes in the electrocardiogram in response to the single test. There was depression of the RST segment of more than 0·5 mm. in 25 (8%) of the 311 subjects after the single or double test or both. The change was most frequently recorded in leads V4 or V5 immediately after the test exercise, and usually disappeared in one or two minutes. In no instance did a T wave become inverted following the test.

The authors state that the results obtained with these tests in patients suspected of suffering from coronary disease should be interpreted only in the light of the patient's history and the physical findings. Follow-up investigation of such patients, however, suggests that a negative cardiographic response indicates a more favourable prognosis. *T. Semple*

1602. **Cardiac Aneurysms: Clinicopathologic Studies**
W. S. PHARES, J. E. EDWARDS, and H. B. BURCHELL. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **28**, 264–271, May 6, 1953. 3 figs., 3 refs.

Out of 40 specimens of ventricular aneurysm in the pathology registry of the Mayo Clinic for the years 1916–51, 31 were located anteriorly, involving the apex, anterior wall, and the septum, and the remainder were posterior. Two only were calcified. Endocardial thrombi and pericardial adhesions were present in two-thirds of the specimens. The ages of the patients varied from 37 to 85 years. In one-quarter only had adequate rest been enjoined after infarction, while in half the cases there was no clinical history of infarction and presumably the patient had not rested at all. In the electrocardiogram in all the cases of anterior aneurysm in which precordial leads had been taken, QS waves and raised S–T segments were present.

The causes of death in the 40 cases were: congestive heart failure (16); acute coronary disease, often with recurrent infarction (15); and peripheral emboli (2). Causes not related to the cardiovascular system, such as carcinoma, accounted for 7 deaths. In no instance did the aneurysm rupture. *C. W. C. Bain*

1603. **The Use of Diamox, a Carbonic Anhydrase Inhibitor, as an Oral Diuretic in Patients with Congestive Heart Failure**
C. K. FRIEDBERG, R. TAYMOR, J. B. MINOR, and M. HALPERN. *New England Journal of Medicine* [*New Engl. J. Med.*] **248**, 883–889, May 21, 1953. 3 figs., 19 refs.

The property of inhibition of carbonic anhydrase activity in the renal tubule cells, which impairs the tubular excretion of hydrogen ions and diminishes the reabsorption of sodium, is possessed by the sulphonamides, and notably by a new compound, " diamox " (2-acetylamino-1 : 3 : 4-thiadiazole-5-sulphonamide).

The authors have investigated the diuretic effect of diamox, given by mouth, on patients with cardiac oedema at Mount Sinai Hospital, New York. Eleven in-patients were given diamox after a control period of 1 or 2 days after admission, rest in bed, sodium restriction, and digitalis therapy being employed concurrently. Diamox was also given by mouth to 15 out-patients in place of the mercurial diuretics which they had been receiving regularly. Doses of 0·25 to 0·75 g. were given, either 8-hourly for 2 or 3 days at a time or once daily for longer periods.

Among the in-patients there was an average increase in urine volume of 737 ml. a day, an average increase in sodium excretion of 86 mEq. a day, and an average weight loss over 3 or 4 days of 2 kg. All but one patient responded favourably. Nine out-patients showed a similar favourable response, but in the remaining 6 diuresis was unsatisfactory and mercurial therapy had to be resumed. The only side-effects experienced with the drug were mild drowsiness and paraesthesiae. The conditions of the experiment were not such as to allow definite conclusions to be drawn, but in the authors' opinion the increase in excretion of water and sodium and the clinical improvement brought about by diamox in cases of cardiac oedema is comparable to that produced by the injection of mercurial diuretics.

Bernard Isaacs

1604. **Recurrent Parietal Thromboendocarditis**

C. McNicol, H. E. MacMahon, A. S. Benenson, and T. Winship. *Circulation* [*Circulation* (*N.Y.*)] **7**, 497–502, April, 1953. 3 figs., 13 refs.

The authors describe in detail 2 cases of a relatively rare endomyocardial affection occurring in young adult males who died in congestive failure. Both were found at necropsy to have gross thickening of the endocardium due to the deposit of collagen therein, with extensive mural thrombosis. The coronary arteries and the valves were normal. The clinical picture was that of low blood pressure and tachycardia with gallop rhythm. A similar condition occurring in Africans has been previously reported by Bedford and Konstam (*Brit. Heart J.*, 1946, **8**, 236), among others. The aetiology is unknown.

C. W. C. Bain

1605. **Alcoholic Enlargement of the Heart (Alcoholic Myocarditis).** (Les gros cœurs alcooliques (myocardie alcoolique))

E. Merle and J. Belin. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **29**, 1454–1462, May 2, 1953. 2 figs., 23 refs.

The observations described in this paper were made in the Auvergne district of France where heavy consumption of alcohol in the form of wine is common, up to 10 litres per day being not rare among viniculturists and 3 litres almost the rule. The effect on the heart as found clinically, radiologically, and electrocardiographically is described and illustrated by short case-histories of 11 patients. The association with alcoholic cirrhosis is briefly discussed, and it is pointed out that neurological lesions are rarer in those addicted to this type of alcoholic drink than in those addicted to spirits. Pathologically, interstitial oedema of the myocardium is considered the essential lesion, confirming the opinion of Marchal.

The various stages of the breakdown of alcohol are restated, and the importance of pyruvic acid and acetaldehyde as toxic substances is emphasized. The similarities and differences between the cardiac conditions produced by alcohol and by aneurin deficiency are discussed. The vitamin deficiency in patients with alcoholic myocarditis is considered to be more complex than that in beri-beri. It is stressed that all the constituents of the vitamin-B complex should be used in the treatment of patients with cardiac lesions due to alcohol, but even so the results are less satisfactory and more transient than those achieved in cases of beri-beri.

A. Schott

1606. **The Innervation of the Heart**

G. A. G. Mitchell. *British Heart Journal* [*Brit. Heart J.*] **15**, 159–171, April, 1953. 10 figs., bibliography.

This paper describes in some detail the origins, pathways, and connexions of the sympathetic and parasympathetic nerve fibres supplying the heart, and their communications with other nerves. The available information about the cardiac plexus, its ganglia, and the mode of termination of its fibres is reviewed.

[This paper should be read in the original, as it cannot satisfactorily be condensed.] *C. Bruce Perry*

1607. **The Clinical Significance of Apical and Aortic Systolic Heart Murmurs (without Diastolic Murmurs) as Heard with the Stethoscope**

P. D. White, R. S. Schaaf, T. B. Counihan, and B. Hall. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **225**, 469–474, May, 1953. 1 ref.

A follow-up study was made of 1,777 patients attending a private cardiac consulting practice, all of whom had slight to moderate systolic murmurs heard best at the cardiac apex or at the aortic area, but without diastolic murmurs. They were compared with 187 patients with loud and very loud systolic murmurs at the same sites, and with 200 patients without murmurs.

Patients with coronary and hypertensive heart disease were the commonest in all 3 groups, but rheumatic heart disease occurred in 27% of those with loud murmurs, 3% of those with lesser murmurs, and in none of those without murmurs. Apical systolic murmurs occurred 5 times more often than aortic murmurs. Patients with the loudest murmurs lived shorter lives than those with lesser murmurs, although 8% of those with the loudest murmurs lived for more than 15 years. Other important factors unfavourably affecting the prognosis were the presence of degenerative rather than rheumatic disease, occurrence in the male, and the presence of cardiac enlargement. An aortic systolic murmur of any grade of intensity gave no worse prognosis *per se* than the corresponding apical systolic murmur. Heart size was the most important single factor affecting the prognosis in all 3 groups of patients. *Keith Ball*

CONGENITAL HEART DISEASE

1608. Analysis of 50 Cases of Persistent Ductus Arteriosus

F. STARER. *British Medical Journal* [*Brit. med. J.*] 1, 971–973, May 2, 1953. 9 refs.

During a 4-year period 53 patients were admitted to the Thoracic Surgical Unit, Leicester, for ligation of a patent ductus arteriosus. One patient developed spontaneous obliteration of the ductus, another had an infected ductus that cured itself spontaneously, and a third patient was found at operation to have an obliterated ductus and a probable rupture of the sinus of Valsalva. The other 50 patients, of whom 45 were females, underwent routine operation. The average age was 9 years and the range 3 to 40 years. All but 4 cases had been diagnosed before symptoms developed. Of 11 patients subjected to the exercise test, 8 showed a fall in diastolic pressure. Associated defects were spina bifida, subaortic stenosis, ventricular septal defect, minor narrowing of the aorta, and left superior vena cava with arachnodactyly. Of the 50 patients, 33 were not incapacitated; one had palpitation, one had heart failure, 9 had symptoms due to bacterial endarteritis, and the activity of the remaining 6 had been unnecessarily restricted by over-anxious parents. All had a machinery murmur, although in one case it disappeared intermittently after infection occurred, this change being associated with cyanosis. On the whole, enlargement of the heart as seen radiologically tended to be correlated with the presence of bacterial endarteritis.

Operation was by ligation without division of the ductus. No recurrences were observed. There was one postoperative death, due it was thought to the inefficient maintenance of an airway after operation at a time of shortage of trained nursing staff. Minor sequelae of operation were: postoperative lung collapse requiring bronchoscopy (2 cases), pulmonary infarct in an infected case, pleural effusion (4 cases), and mild wound infection (one case); all these patients eventually did well. The author considers 7 years a good age for operation.

K. G. Lowe

1609. Congenital Aortic Valvular Stenosis

M. CAMPBELL and R. KAUNTZE. *British Heart Journal* [*Brit. Heart J.*] **15**, 179–194, April, 1953. 14 figs., 23 refs.

The authors report a series of 40 cases of aortic stenosis which was believed to be congenital in origin. In 20 the murmur was heard in early childhood, but symptoms developed late, only 9 patients having more than slight dyspnoea and most of these being over 30 years of age. A systolic thrill was felt at some time in all 40 cases but varied in position, being felt above the sternal notch, at the pulmonary area, and even at the apex beat in different cases. The aortic sound was weak or absent in half the cases, but was normal or loud even in some patients with calcification of the valves. Generally the heart was little enlarged, but fluoroscopy usually revealed some left ventricular enlargement and often some dilatation of the first part of the aorta. Calcification of the valve was seen in 11 cases, the youngest patient to show this being 18.

The electrocardiogram in this condition may be normal for years, but sooner or later shows evidence of left ventricular strain. A vertical electrical axis with evidence of left ventricular preponderance and strain in the absence of mitral stenosis is suggestive of congenital aortic stenosis. *C. Bruce Perry*

1610. Idiopathic Congenital Dilatation of the Pulmonary Artery

B. M. KAPLAN, J. G. SCHLICHTER, G. GRAHAM, and G. MILLER. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **41**, 697–707, May, 1953. 4 figs., 13 refs.

The clinical diagnosis of idiopathic congenital dilatation of the pulmonary artery has until recently been difficult to establish. Little is known of its pathology, prognosis, or treatment. The authors present 6 fully investigated cases of this condition seen at the Michael Reese Hospital, Chicago, and discuss the differential diagnosis.

Symptoms were remarkably absent, the patients being referred for investigation because murmurs had been heard. In no case was there cyanosis, clubbing, chest deformity, habitus gracilis, or heart failure. The second pulmonary sound was always accentuated. In each case there was a basal systolic murmur, sometimes accompanied by a thrill. The remarkable feature of the murmur was its inconstancy, all the classifying features tending to change from time to time in a given patient. In 3 patients a short, inconstant, diastolic murmur was heard. Radiological examination showed the pulmonary artery to be enlarged and dynamic in all cases, but the " hilar dance " was not noted. The peripheral vascular markings were all normal. There was no abnormality of any chamber of the heart or of the aortic knob. Electrocardiograms were normal and there was no evidence of any general arterial disease.

Cardiac catheterization and blood oxygen studies showed that no shunt existed in either direction and that all pressures were normal. Cardiac output and cardiac index values also were normal. Full respiratory studies gave normal results.

The authors regard as characteristic of the condition the isolated finding of an inconstant basal systolic murmur and pulmonary arterial dilatation on *x*-ray examination with screening. A full and accurate differential diagnosis from the other important forms of acyanotic, asymptomatic, congenital heart disease, in the form of a table, is included. *H. David Friedberg*

1611. Idiopathic Dilatation of the Pulmonary Artery

R. H. GOETZ and M. NELLEN. *South African Medical Journal* [*S. Afr. med. J.*] **27**, 360–367, May 2, 1953. 9 figs., 19 refs.

The authors review the literature regarding idiopathic dilatation of the pulmonary artery and describe 4 cases of their own. The physical signs included a systolic murmur, varying in intensity, in the pulmonary area (in one case a diastolic murmur was also present) and a

normal or accentuated pulmonary element of the second heart sound. In one case the second sound was duplicated in the pulmonary area. Cyanosis and clubbing were absent in every case. Fluoroscopy revealed enlargement of the main pulmonary artery and some enlargement of the right ventricle. Electrocardiograms were normal and cardiac catheterization did not demonstrate any left-to-right shunt, while the pressure in the right ventricle and pulmonary artery was normal. Angiocardiography, which was performed in 3 cases, confirmed the enlargement of the main pulmonary artery, but the result was otherwise normal.

In the authors' view idiopathic dilatation of the pulmonary artery must be considered in the differential diagnosis of any patient with a systolic and/or diastolic murmur in the pulmonary area and enlargement of the pulmonary artery. Cardiac catheterization and perhaps angiocardiography are necessary to make the diagnosis with certainty, and in particular to exclude atypical cases of atrial or ventricular septal defect, patent ductus arteriosus, pulmonary hypertension, and pulmonary stenosis. The authors point out, however, that the differential diagnosis between pulmonary stenosis of slight degree and idiopathic dilatation of the pulmonary artery may be exceedingly difficult, since it has been shown elsewhere that in both conditions the systolic pressure in the pulmonary artery may be slightly lower than in the right ventricle. *J. F. Goodwin*

CHRONIC VALVULAR DISEASE

1612. **Influence of Tolazoline Hydrochloride (Priscol) on Cerebral Blood-flow in Patients with Mitral Stenosis**
H. A. DEWAR, S. G. OWEN, and A. R. JENKINS. *Lancet* [*Lancet*] **1**, 867–870, May 2, 1953. 3 figs., 19 refs.

Some workers have observed that administration of tolazoline ("priscol") is followed by a sensation of fullness in the head and dilatation of the retinal vessels, suggesting that the brain may participate in the increased blood flow produced by the drug, while other workers have reported improvement in patients with cerebral ischaemia after treatment with tolazoline. The present authors, at the Royal Victoria Infirmary, Newcastle upon Tyne, and King's College, University of Durham, have estimated cerebral blood flow by the nitrous oxide method before and after intravenous injection of this drug in 6 patients with mitral stenosis. A cardiac catheter was inserted into the internal jugular vein and advanced to the base of the skull, and an indwelling needle placed in the brachial or femoral artery. The patient then breathed a mixture containing 15% N_2O, and blood samples were taken simultaneously from the artery and vein at timed intervals or by continuous withdrawal. In this way the integrated arterio-venous nitrous oxide difference could be determined with a Van Slyke manometric apparatus for gas analysis, and, by application of the Fick principle, the mean cerebral blood flow per 100 g. of brain tissue estimated. If the mean arterial blood pressure was known, the cerebral vascular resistance could also be calculated. About 30 minutes after the initial blood-flow determination 20 to 30 mg. of tolazoline was given intravenously and a second determination made.

In all patients there was a significant increase in cerebral blood flow, averaging 25%, accompanied by a fall in cerebral vascular resistance. The authors suggest that the action of tolazoline on the cerebral circulation is like that of histamine, differing from the latter in that the effective cerebral arterial pressure is maintained, with a resultant increase in cerebral blood flow.

[The procedure described would seem to be unnecessarily long, in that tolazoline could be administered during the initial blood-flow determination, thus obviating the delay between the two observations.] *A. Paton*

1613. **The Lung in Mitral Disease.** (Le poumon des mitraux)
P. SOULIÉ, J. BAILLET, J. CARLOTTI, P. CHICHE, R. PICARD, M. SERVELLE, and G. VOCI. *Archives des maladies du cœur et des vaisseaux*. [*Arch. Mal. Cœur*] **46**, 393–422, May, 1953. 9 figs., 49 refs.

The authors present a long and detailed discussion of the anatomical and histological findings in the lungs in 12 fatal cases of mitral stenosis studied at the Hôpital Lariboisière, Paris. The normal and morbid histology of the lungs and their vessels are fully described. The dominant lesion is narrowing, and sometimes thrombosis, of the precapillary arterioles, in which the intima is hypertrophied, has a desquamated appearance, and is surrounded by concentric layers of muscle fibres; there is no adventitial reaction. The abnormal areas of parenchyma are disposed irregularly throughout the lung and exhibit reticular hypertrophy. The alveoli are empty and not congested. The alveolar septa are thickened by organized connective tissue which buries the capillaries and reduces the respiratory surface. In many cases the alveoli are relined by cubical epithelium which impairs respiratory exchange, and between the alveoli is oedematous tissue containing macrophages. There is accompanying lymphadenopathy, and often haemosiderosis and infarction.

Among the haemodynamic changes observed were an increased pulmonary arteriolar resistance, from 240 to 1,220 Wiggers units, a pulmonary capillary pressure of 20 to 30 mm. Hg, a right ventricular pressure of 60/5 to 135/15 mm. Hg, and a mitral area of 0·7 to 1 sq. cm. The raised pulmonary arterial pressure is not due to generalized vasoconstriction, but to obstruction of the precapillary arterioles and muscular arteries in the areas of reticular hypertrophy. The raised pressure permits respiratory exchange in the normal areas, so that there is relatively little unsaturation. The probable origin of the reticular hypertrophy is that mitral stenosis causes raised left auricular pressure leading to raised capillary pressure and hence exudation, resulting in intraseptal oedema and eventual sclerosis. An abnormal number of anastomoses were found between branches of the pulmonary and bronchial arteries, with collaterals joining the submucous bronchial veins. The pulmonary hypertension causes dilatation and rupture of these bronchial veins, resulting in haemoptysis.

The sequence of the haemodynamic changes is as follows. Mitral stenosis causes a fall in cardiac output unless compensated by a rise in left auricular and capillary pressures. Up to a point, there are no clinical ill effects, but when the mitral area is less than 1·5 sq. cm. the capillary pressure exceeds the plasma filtration pressure. Compensatory mechanisms which then come into play are distension of the left auricle and a fall in cardiac output. If these mechanisms fail early, the result is acute pulmonary oedema: if late, intra-septal oedema. There are thus two corresponding clinical types of stenosis, the oedematous and the dyspnoeic. The oedematous type usually occurs in young subjects, with sinus rhythm, normal heart volume, little dyspnoea, increased hilar blood flow, and a fairly normal electrocardiogram; catheterization shows a raised capillary pressure. Progressive pulmonary oedema is a strong indication for valvotomy. The second type starts with dyspnoea on exertion, with or without paroxysms of oedema, and leads to permanently impaired exercise tolerance, with gross dyspnoeic crises. Radiography shows emphysematous lung fields, with an enlarged heart and dilated conus, and electrocardiography gives evidence of right ventricular preponderance.

In selecting dyspnoeic cases for operation, differentiation must be made between the roles played by mitral and arteriolar obstruction respectively. The prognosis is best when pulmonary circulation is least affected and reticular tissue least modified, so that after the operation areas previously avascular and non-aerated can be utilized. In practice, important information may be obtained by observing the patient during the induction of anaesthesia. As curare and oxygen tend to relieve the arteriolar obstruction, the appearance or increase of cyanosis, which means that blood is being conducted to grossly affected areas of lung, indicates a poor prognosis. Delayed postoperative improvement in exercise tolerance suggests that arteriolar obstruction may at least in part be due to spasm rather than to anatomical narrowing.

D. Goldman

1614. **The Opening Snap of Mitral Stenosis**

P. MOUNSEY. *British Heart Journal* [*Brit. Heart J.*] 15, 135–142, April, 1953. 7 figs., 18 refs.

As confusion may arise between the " opening snap " of the mitral valve and the second component of the second heart sound, or the physiological third heart sound, 33 cases of mitral stenosis were examined clinically and phonocardiographically at the London Hospital to determine the character and any clinical signs of these sounds which might help in their recognition and differentiation. In 28 cases it was diagnosed clinically and confirmed by the phonocardiogram; in 4 of the remaining 5 cases it was demonstrated graphically but could not be recognized clinically with certainty.

The opening snap was best heard in the supramammary area (above and a little internal to the left nipple), and was also often well heard in the mitral area or at the lower left sternal border; the second component of the second heart sound was best heard in the pulmonary area. The time interval between the second sound and the opening snap varied from 0·03 to 0·14 second (average 0·07 second), whereas the interval between the two components of the split second sound varied between 0·01 and 0·05 second (average 0·03 second). The normal third heart sound had a lower frequency than the opening snap and occurred 0·16 to 0·24 second after the second heart sound; it was best heard just inside the mitral area. The opening snap was absent or not well heard in one case in which the degree of mitral stenosis was mild and in 3 cases in which the valve was grossly calcified or extremely rigid. The opening snap is a valuable sign, and if heard alone should prompt a further search for a diastolic murmur. A clear third heart sound was not recognized clinically in any of the cases, although it appeared in 8 of the phonocardiograms.

C. Bruce Perry

1615. **Comparison of Operation and Clinical Findings in Mitral Stenosis and Incompetence**

A. VENNER and H. E. HOLLING. *British Heart Journal* [*Brit. Heart J.*] **15**, 205–213, April, 1953. 4 figs., 10 refs.

In the Cardiac Department, Guy's Hospital, London, the state of the mitral valve was assessed directly at operation in 96 patients with mitral valvular disease, and the findings compared with those obtained by clinical examination. In 61 cases there was severe mitral stenosis but no palpable regurgitant stream; the prospects for valvotomy in this group were good. A further 9 patients were found to have larger, rigid orifices with a palpable regurgitant stream, and this group was considered unsuitable for valvotomy. (The remaining 26 patients, who had intermediate degrees of mitral stenosis and regurgitation, were finally excluded from the analysis.)

The clinical, radiological, and electrocardiographic records of these 70 cases were analysed, as well as the findings obtained on catheterization, with a view to establishing means for distinguishing cases suitable for valvotomy from cases in which the predominant lesion was mitral incompetence, for which there would be little prospect of improvement by operation. None of the methods accomplished this, nor could the distinction be made by examination of left atrial pressure tracings or by noting the presence or absence of systolic expansion of the left atrium either at operation or on fluoroscopy. The authors point out that the volume of regurgitating blood in patients with wider, rigid mitral orifices is small in comparison with the volume of the left atrium and pulmonary veins, and is smaller than is usually assumed. They explain this as being due to the obliteration, during ventricular systole, of the interpapillary space and of most of the inflow tract of the left ventricle by the apposition of the papillary muscles and the ventricular wall.

A. Schott

1616. **Gross Calcification of the Mitral Valve**

A. WYNN. *British Heart Journal* [*Brit. Heart J.*] **15**, 214–220, April, 1953. 5 figs., 9 refs.

At St. Thomas's Hospital, London, 60 adult patients with mitral stenosis and evidence of gross calcification of the mitral valve, found fluoroscopically or at necropsy or operation, were studied in respect of duration and

severity of the disease and of the influence of calcification upon heart sounds and murmurs and mitral incompetence; 170 patients with mitral stenosis but without evidence of gross calcification served as controls No significant difference in age incidence between the two groups was found. The incidence of severe mitral-valve disease tended to be higher in the patients with calcification, but 15% had only mild symptoms. Apical systolic murmurs were twice as frequent in those with calcification than in those without, but in 5 patients with gross calcification such murmurs were absent. Opening snap was demonstrable in 48% of the group with calcification as compared with 82% of the control group.

The author emphasizes that, owing to the many variables involved, the value of these observations is limited. *A. Schott*

PERIPHERAL ARTERIES

1617. **Studies in Peripheral Arterial Occlusive Disease. I. Methods and Pathologic Findings in Amputated Limbs**
S. WESSLER and M. J. SCHLESINGER. *Circulation* [*Circulation (N.Y.)*] **7**, 641–655, May, 1953. 5 figs., 20 refs.

A new technique for studying the arterial circulation in amputated limbs is described in this paper from the Beth Israel Hospital and Harvard University, Boston. It consists in the injection of the arterial tree with a radiologically opaque substance containing lead and gelatin, the precise composition of which, and also the method of injection, are described in detail. The soft tissues of the limb are unrolled so that the vessels of the posterior aspect of the limb are not superimposed on the vessels of the anterior aspect. Radiographs are taken before and after injection and again after the unrolling.

The findings in 72 amputated legs are described. It appears that arterial obstruction in arteriosclerosis is much more common in the vessels below the knee than in the femoral or popliteal arteries. The posterior tibial artery is the first artery to be occluded, but before gangrene develops arterial obliteration must be widespread, as the collateral circulation in the leg is very free and can compensate for limited arterial obstruction. The authors believe that the collateral vessels are already preformed in the normal limb, and that they enlarge with the stimulus of main-trunk obliteration. Calcification of vessels bears no relationship to the incidence of vascular obliteration: in fact, there appears to be an inverse relationship between calcification and arterial thrombosis.

[This is a full and detailed description of an important investigation of a very common disease. Undoubtedly a great deal could be learned from further such studies.] *Peter Martin*

1618. **Heparin in the Treatment of Arteritis of the Lower Limbs.** (L'héparine dans le traitement des artérites des membres inférieurs)
M. RÉMY, P. CADIOT, and C. PERNOT. *Presse médicale* [*Presse méd.*] **61**, 961–962, July 4, 1953.

1619. **Recanalization of Thrombosed Arteries under Anticoagulant Therapy**
H. PAYLING WRIGHT, M. M. KUBIK, and M. HAYDEN. *British Medical Journal* [*Brit. med. J.*] **1**, 1021–1023, May 9, 1953. 4 figs., 10 refs.

A method of inducing thrombosis experimentally in the femoral artery of the rabbit is described in this paper from University College Hospital Medical School, London, the basis of the method being the isolation of three contiguous segments of femoral artery and the injection of thrombin into the middle segment and of sodium morrhuate into the proximal and distal segments.

Thrombosis was induced in this way in two groups of animals, one of them acting as a control group and the other being treated after 24 hours with "tromexan" (ethyl biscoumacetate) by mouth to achieve a prothrombin time of 30 minutes, the state of the vessel being observed from time to time in each group by arteriography. In all 6 animals in the untreated control group the femoral vessel remained obstructed after 8 weeks, but in the group treated with tromexan the average time for recanalization to occur was 3·25 weeks. Histological examination of the arteries of both groups of animals was made after patency of the femoral artery had been established by arteriography in the treated group. A section of a previously obstructed artery showed nothing but a small mural thrombus and, apart from this, a normal intima. On the other hand, all sections of untreated thrombosed vessels showed typical organizing thrombus with no recanalization.

In discussing these results the authors suggest that it may be that the normally continuous action of fibrinolysin may, in the untreated case, be masked by the continuous deposition of fresh fibrin on the surface of the clot, an action which is inhibited by anticoagulants; or possibly an inhibition of fibroblasts (which has been shown to occur in tissue culture with dicoumarol) may be the operative factor.

[The results of the clinical application of these findings in cases of sudden arterial occlusion will be awaited with great interest.] *Peter Martin*

HYPERTENSION

1620. **Observations on Prognosis in Hypertension**
A. W. D. LEISHMAN. *British Medical Journal* [*Brit. med. J.*] **1**, 1131–1135, May 23, 1953. 5 figs., 9 refs.

The object of this investigation at the United Sheffield Hospitals was to define any factors which would enable prognosis to be determined at the first examination of a patient with hypertension. The patient with benign or malignant hypertension can usually be recognized, but it is difficult to pick out the subject in whom the disease will take an "accelerated" course—that is, one that is more rapid than that of benign hypertension, but less precipitate than that of malignant hypertension. For purposes of the study 151 patients with hypertension (93 female and 58 male), under 60 years of age and with a diastolic blood pressure of 100 mm. Hg or more, have been followed up for 2½ to 5 years. Investigations

included retinoscopy, intravenous pyelography, 6-foot (1·8-m.) radiograph of the chest, 12-lead electrocardiography, examination of the urine and a modified urine concentration test, and standard blood biochemistry.

During the period of observation 51 patients (34%) died as a result of the hypertension, the mortality in men alone being 44%. Most of the deaths occurring under the age of 45 were due to uraemia, and most of those from other causes fell in the sixth decade. An accelerated course was usual in patients whose diastolic pressure was over 130 mm. Hg, and among 27 patients with severe hypertension of this kind, as compared with 73 in whom the diastolic pressure was lower, cardiac enlargement, an abnormal electrocardiogram (ECG), gross retinal changes, and angina were commoner. There was no significant difference in the incidence of headache or albuminuria between the two groups. Deterioration was found most commonly to have its onset in a cerebral vascular accident. In an attempt to recognize the factors which may lead to this complication, the initial findings in 30 patients who subsequently had strokes were compared with those in 17 patients with severe hypertension but without such accidents. This showed a higher incidence in the former of enlarged heart, abnormal ECG, advanced retinal changes, and albuminuria—that is, the arterial disease was more advanced, although in many cases the hypertension was not of such a severe degree.

Analysis of the initial findings in the 20 patients who died in uraemia showed that a large number had advanced retinal changes and albuminuria, although in only a little over 50% of them was the blood pressure severely raised at this time; cardiac enlargement and an abnormal ECG were comparatively uncommon.

The author is of the opinion that if a hypertensive subject is investigated in the way described it should be possible to determine how much damage has already been done and to decide whether the course will be benign or accelerated. *Arthur Willcox.*

1621. **The Clinical Results of Oral and Parenteral Administration of 2-(N′-*p*-Tolyl-N′-*m*-hydroxyphenylaminomethyl) Imidazoline Hydrochloride (Regitine) in the Treatment of Hypertension and an Evaluation of the Cerebral Hemodynamic Effects.**
J. H. Moyer and C. Caplovitz. *American Heart Journal* [*Amer. Heart J.*] **45**, 602–610, April, 1953. 2 figs., 9 refs.

"Regitine" is the hydrochloride of an imidazoline compound related to tolazoline ("priscol") and has marked adrenaline and adrenergic blocking activity. To evaluate its usefulness in the relief of hypertension, 48 out-patients were studied at the Baylor University College of Medicine, Houston, Texas. After a control period of 1 to 3 months they were given the drug by the oral, the intramuscular, or the intravenous route. During the control period and that of drug administration the blood pressure was recorded in both the supine and the prone position. At first, 16 patients received 1 to 2 mg. of regitine per kg. body weight intravenously twice weekly for 2½ weeks, the remaining 32 receiving 1 mg. per kg. daily or twice daily intramuscularly for 4 days. After this preliminary period for assessment of responsiveness, 16 of the latter group continued to receive regitine intramuscularly in the same dosage for 3 months or more, while to 24 of the remaining 32 patients the drug was given orally in an initial dose of 50 mg. 6-hourly, this being increased, according to individual tolerance, to a maximum dose ranging from 100 to 900 mg. per day.

In the initial period, in 45 (94%) of the patients the blood pressure was reduced by parenterally administered regitine. After 3 months, however, resistance to the drug given intramuscularly developed and in only 6 of the 16 patients could a hypotensive response (defined as a reduction of over 20 mm. Hg in the diastolic pressure) be elicited. With oral administration intolerable gastrointestinal symptoms developed in all patients. Other frequently observed side-effects after administration by all of the three routes were tachycardia, "stuffy nose", weakness, and dizziness. It was concluded that regitine should be used only for short-term therapy, such as is required for a hypertensive crisis or as interval therapy between courses of other hypotensive agents; it should then be given by the intramuscular route.

As with other hypotensive drugs, it was found that when the cerebral blood flow was estimated by the nitrous oxide method the flow was maintained despite a reduction in blood pressure. Since the same effect was found with preparations of veratrum viride, which does not produce blockage of the sympathetic nervous system, it was concluded that this phenomenon was not produced by adrenergic blockage. These findings support the suggestion made by other authors that adjustments of cerebral haemodynamics are such that the partial pressures of oxygen and carbon dioxide remain constant.
Robert Hodgkinson

1622. **"Dibasol" in Hypertensive Disease.** (Применение дибазола при гипертонической болезни)
E. V. Stupina *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **31**, 47–50, Jan., 1953. 5 refs.

A new Russian preparation, "dibasol", a heterocyclic compound linked with a benzene radical, has been extensively used in the U.S.S.R. for the treatment of hypertension and certain other diseases. Its mode of action appears to be in doubt, some authorities claiming for it a stimulant action on the central nervous system at levels below the cerebral cortex, but none on the cortex itself, and others a purely vasodilator action upon the arterial musculature. The present article describes an investigation into the effect of dibasol in cases of hypertensive disease by means of oscillography and measurements of brachial and temporal arterial pressure, venous pressure, and circulation time. In all, 46 patients with hypertension and 15 normal controls were examined; 8 of the patients were in the first stage of the disease (with transient hypertension), 21 in the second (with permanent hypertension), and 17 in the third stage (with arteriosclerotic changes).

Dibasol was administered either subcutaneously (2 ml. of 1% solution) or by mouth as a powder (·05 g.). By injection it produced a fall of arterial pressure within

5 minutes, its effect reaching a maximum in 40 minutes. Oral administration produced a similar effect in 40 to 80 minutes. The average fall was 25 mm. Hg in the systolic and 10 mm. in the diastolic pressures in the brachial artery, but rather less in the temporal artery. The effect on venous pressure was variable and could not be related to the stage of the disease or the conditions of treatment, the pressure sometimes being reduced, sometimes raised, and in some cases unaffected. The circulation time remained on the average within the lower limit of normal. Relief of symptoms, especially headache and vertigo, was rapid. The effects of the drug were more noticeable in the earlier stages of the disease.

L. Firman-Edwards

1623. **Electrocardiographic Changes in Patients with Hypertensive Disease and Angina Pectoris after Treatment with "Dibasol".** (Динамика электрокардиограммы у больных гипертонической болезнью и грудной жабой при лечении дибазолом)

N. N. SEGAL. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **31**, 51–55, Jan., 1953. 1 fig., 7 refs.

A series of 100 men, 25 with hypertensive disease, 23 with angina pectoris, and 52 with both, were treated with "dibasol" [see Abstract 1622]. Of the patients with angina, 29 with hypertension and 16 of the remainder had pain even at rest. Dibasol was given twice or three times daily, 2 hours after food, over an average period of 15 days, no other drug being given during the investigation. Electrocardiographic records were taken before treatment, after 1 week, and at the end of the course.

The results were very satisfactory, only one patient failing to respond. The best results were obtained in early cases. The anginal attacks were diminished in frequency, disappearing altogether in 37 cases and becoming shorter and less severe in 38. The blood pressure fell in both hypertensive and normotensive patients, but more in the former. The electrocardiogram tended to become normal, especially as regards rhythm, shortening of ventricular systole, and return of S–T to the isoelectric level. In those patients examined a month later the changes were maintained. No side-effects of the drug were observed.

L. Firman-Edwards

PORTAL CIRCULATION

1624. **Assessment of Portal Venous Hypertension by Catheterization of Hepatic Vein**

A. PATON, T. B. REYNOLDS, and S. SHERLOCK. *Lancet* [*Lancet*] **1**, 918–921, May 9, 1953. 4 figs., 13 refs.

At the Postgraduate Medical School of London portal venous pressure was measured in patients with and without hepatic disease by the occlusion of a hepatic vein with a radio-opaque catheter in a similar fashion to that employed in measuring pulmonary venous pressure, the catheter being passed via an antecubital vein about 10 cm. into the hepatic vein, to the periphery of the liver. In some patients the pressure was also measured through 1-mm. polythene tubing tied into a tributary of the portal vein at subsequent operation and left *in situ* for a few days.

Pressure measurements from different tributaries of the hepatic vein showed good agreement both with each other and with subsequent measurements from a portal tributary. The mean pressure in 24 subjects without hepatic disease was 6·8 mm. Hg (standard error $\pm$0·49 mm. Hg), the highest reading being 11·2 mm. Hg, while the mean pressure in 11 patients with portal cirrhosis was 22·0$\pm$1·94 mm. Hg. Pressures in the unobstructed hepatic vein were also higher in portal cirrhosis. The hepatic venous pressure was normal in 3 patients with clinical evidence of portal hypertension in whom extrahepatic portal obstruction was subsequently diagnosed at operation, in 4 with extrahepatic biliary obstruction, and in 3 with intrahepatic biliary obstruction (primary biliary cirrhosis). In 2 patients with subacute infective hepatitis the pressure was above the normal range, suggesting that there was already some distortion of lobules and fibrosis. The hepatic venous pressure was high in 4 patients with congestive heart failure. There was no difference in oxygen saturation of hepatic venous blood from patients with and without cirrhosis, and there was thus no evidence of a hepatic arterio-venous shunt in the former.

The good agreement between the pressures recorded from an occluded hepatic vein and those measured direct from the portal vein shows that hepatic arterial pressure does not affect the pressure in the occluded hepatic vein. In practice the method has proved satisfactory for assessing portal hypertension, determining the site of obstruction, and following the results of surgical treatment.

Albert Venner

1625. **The Measurement of Liver Circulation by Means of the Colloid Disappearance Rate. I. Liver Blood Flow in Normal Young Men**

E. L. DOBSON, G. F. WARNER, C. R. FINNEY, and M. E. JOHNSTON. *Circulation* [*Circulation (N.Y.)*] **7**, 690–695, May, 1953. 2 figs., 8 refs.

When colloidal chromic phosphate labelled with the radioactive isotope ^{32}P is injected into the blood stream the colloid particles are taken up by the phagocytes of the liver. The rate of disappearance of colloid from the blood can be determined by measuring radioactivity in consecutive blood samples. The extent of mixing at any time is gauged from the concentration in the blood of the blue dye T-1824, which is injected simultaneously with the colloidal solution. In a study at the University of California the colloid disappearance-rate constant (k) in 29 healthy fasting men was found to be 0·287$\pm$0·007 minute, the liver blood flow in litres per minute being determined by multiplying the blood volume by k. The authors state that depending upon the value accepted for the blood volume this gives a liver blood flow of from 1·5 to 1·8 litres per minute, and that this agrees almost exactly with liver blood flow values obtained by other workers using different methods.

A. I. Suchett-Kaye

Correction.—In the September issue, page 220, line 9, "Groups 3 and 4" should read "Groups 1 and 2".—[EDITOR]

Haematology

1626. **Collection, Preservation and Transfusion of Platelets. With Special Reference to the Factors Affecting the " Survival Rate " and the Clinical Effectiveness of Transfused Platelets**

M. STEFANINI and W. DAMESHEK. *New England Journal of Medicine* [*New Engl. J. Med.*] **248**, 797–802, May 7, 1953. 4 figs., 15 refs.

Recent technical improvements in the collection of whole blood for transfusion have resulted in less injury to the readily damaged platelets. Judging by the survival of transfused platelets in the recipient as found in an investigation at the New England Center Hospital and Tufts College Medical School, Boston, the authors recommend for the treatment of thrombocytopenia: (1) direct transfusion of polycythaemic (preferably) or normal blood with silicone-coated syringes and needles coated with " arquad 2-C " (dicoco-dimethyl-ammonium chloride); (2) transfusion of blood collected into plastic bags containing an anticoagulant, such as acid citrate dextrose (A.C.D.) or " sequestrene–Na_2 " (disodium ethylenediamino tetra-acetate dihydrate), through plastic tubing; and (3) administration of concentrates of platelets prepared by methods involving the minimum of injury.

Stored platelets suspended in plasma appear to be normal both functionally and morphologically; when suspended in saline they soon manifest staining abnormalities and the inability to restore clot retraction in platelet-poor plasma.

The survival of platelets *in vivo* varies strikingly according to the pathological condition present; there are, for instance, abnormal platelet-destructive mechanisms in idiopathic thrombocytopenic purpura, and development of platelet agglutinins can occur after multiple transfusions.

[In this review of the authors' work the experimental evidence on which the statements are based is not given, but is to be found in previously published work quoted.]

John F. Loutit

1627. **Treatment of Polycythaemia Rubra Vera**

R. BODLEY SCOTT. *British Medical Journal* [*Brit. med. J.*] 1, 1128–1131, May 23, 1953. 3 figs., 11 refs.

From a review of the symptomatology of polycythaemia rubra vera, of the associated conditions present in a series of 36 cases seen during the last 5 years, and of the literature concerning the causes of death in such cases (of which thrombosis is much the most frequent), the author concludes that " restraint of the hyperplastic bone marrow " is a rational aim in the treatment of this disease.

From his own experience and from the results published by workers in the United States he considers that radioactive phosphorus (^{32}P) offers the best means of control of the bone marrow. Of 16 patients treated with ^{32}P at St. Bartholomew's Hospital, London, and observed for at least a year, in 13 (80%) the blood count remained within the normal range during that time, with relief of symptoms, the remaining 3 being resistant to treatment or developing leucopenia or thrombocytopenia. He points out, however, that according to American workers the development of acute leukaemia is much more common in cases of polycythaemia treated with ^{32}P (23·3% mortality) than in those treated by other methods (5·6% mortality).

John F. Wilkinson

1628. **Treatment of Refractory Nutritional Anemia with Gelatine**

C. REICH and M. G. MULINOS. *Bulletin New York Medical College, Flower and Fifth Avenue Hospitals* [*Bull. N.Y. med. Coll.*] **15**, 52–58, 1952. 21 refs.

The authors have treated 20 cases of what they describe as " refractory nutritional anaemia " by the administration of 60 g. of gelatin daily in the diet. [They state that " all subjects had reached a plateau of reactivity to iron, etc., as to their anemia, hence were considered as refractory ", but no clinical details are given apart from the statement that patients were " free of any taint of injury to or disease of the hemopoietic system ".] The mean haemoglobin percentage rose from 68·6 to 73·1, the number of erythrocytes from 3,500,000 per c.mm. to 3,840,000 per c.mm., and the reticulocytes from 0·36 to 0·56%. The evidence for new blood formation was considered to be " unequivocal ". The gelatin was given daily for 4 to 6 weeks together with iron, vitamins, and a good diet. The authors consider that the gelatin supplied some amino-acid, probably glycine, essential for haematopoiesis.

Janet Vaughan

1629. **Paroxysmal Nocturnal Hemoglobinuria. Plasma Factors of the Hemolytic System**

W. H. CROSBY. *Blood* [*Blood*] **8**, 444–458, May, 1953. 1 fig., 11 refs.

The nature of the factor or factors in normal serum which haemolyse the erythrocytes in paroxysmal nocturnal haemoglobinuria (P.N.H.) has for long been a matter of interest and speculation. In this paper from the Walter Reed Army Medical Center, Washington, D.C., the author underlines the complexity of the problem by presenting experimental evidence for the existence of 4 factors, 2 being heat-labile and 2 heat-stable. Full details of the method are given. Separation of the factors was achieved by dialysis of serum against distilled water after adjustment of the *p*H to 6·5, and by heating at 56° C. Two of the factors are haemolytic for P.N.H. erythrocytes, one of these being heat-labile and the other heat-stable, and the other two factors act as inhibitors. The heat-labile haemolytic factor is water-soluble, that is, it is not precipitated by dialysis against distilled water, and is slowly inactivated by

thrombin; it is inactive unless a water-insoluble heat-stable haemolytic factor is also present. The heat-labile inhibitor is insoluble in water, but the heat-stable inhibitor is water-soluble and is rapidly destroyed by thrombin. The presence of small amounts of both calcium and magnesium is probably essential.

The author suggests that the intensity of the haemolytic activity of a particular serum againt P.N.H. erythrocytes probably depends upon the balance between the haemolytic factors and the inhibiting factors. He also considers the possible relationship between the factors he describes and serum complement, but is unable to arrive at any firm conclusions as to their possible identity.

J. V. Dacie

1630. **Serological Findings in a Case of Haemolytic Anaemia. With Some General Observations on the Pathogenesis of this Syndrome**
W. WEINER, D. A. BATTEY, T. E. CLEGHORN, F. G. W. MARSON, and M. J. MEYNELL. *British Medical Journal* [*Brit. med. J.*] **2**, 125–128, July 18, 1953. 10 refs.

See also Pathology, Abstract 1498.

HAEMORRHAGIC DISEASES

1631. **Haemorrhagic Diathesis due to Absence of Christmas Factor**
S. VAN CREVELD and M. M. P. PAULSSEN. *Lancet* [*Lancet*] **1**, 823–824, April 25, 1953. 18 refs.

The case is described from the Paediatric Clinic, University of Amsterdam, of a boy of 10 years, an only child, who had from infancy shown a haemorrhagic tendency clinically resembling haemophilia. There was no family history of a haemorrhagic tendency. The clotting time of venous blood was prolonged; prothrombin consumption was much below normal; the results of a one-stage prothrombin test were normal; and Factor V was present in normal amounts. On the other hand, it was found that the patient's plasma was able to correct the clotting defect of known haemophilic plasma, and that thromboplastin generation (Biggs and Douglas, *J. clin. Path.*, 1953, **6**, 23) was defective. *A. Brown*

1632. **A New Method for the Diagnosis of Haemophilia. The Estimation of Antihaemophilic Factors A and B.** (Nouvelle méthode de diagnostic de l'hémophilie. Dosage des facteurs antihémophiliques A et B)
J. P. SOULIER and M. J. LARRIEU. *Sang* [*Sang*] **24**, 205–215, 1953. 3 figs., 11 refs.

Writing from the Centre National de Transfusion Sanguine, Paris, the authors describe a specific test for the quantitative measurement of the antihaemophilic activity of the blood. In one patient they detected an apparently new factor, which they have called Factor B.

The reagent for Factor A is prepared from the oxalated plasma of a typical haemophiliac by repeated centrifugation in the cold, and is free of platelets and thromboplastin. It has a full complement of prothrombin, proconvertin, and most of the original pro-accelerin. The platelet factor is prepared from fresh normal citrated plasma. By centrifugation in the cold a platelet clot is obtained which is resuspended in distilled water, heated to destroy antihaemophilic activity, and then homogenized by repeated freezing and thawing. The plasma to be tested and a control plasma are obtained from blood collected and treated under the usual conditions and diluted to 1 in 20 immediately before use. The test consists in mixing 0·1 ml. of each of the above and 0·1 ml. of calcium chloride solution in a haemolysis tube in a water bath at 37° C. and noting the time required for clotting.

The test was performed in 18 cases of familial and sporadic haemophilia with varying clotting times but all showing impaired coagulability in a heparin tolerance test and disturbed prothrombin consumption. In all the cases a prolongation of the coagulation time comparable with that of normal plasma diluted 1 in 100 to 1 in 2,000 was found.

In a 19th patient, however, apparently a typical haemophiliac with a similarly affected brother, the test showed a normal coagulation time. A mixture of this patient's plasma with that of a typical haemophiliac gave a normal clotting time, demonstrating that the typical haemophilic plasma contained a factor deficient in this 19th case, and called by the authors Factor B. Factor B was found to be present in normal fresh or old plasma with or without platelets, in normal serum, and in dicoumarinized plasma; it was adsorbed by barium sulphate and resisted a temperature of 56° C. for 5 minutes, but was destroyed at 64° C. A reagent B was therefore prepared from the 19th patient's plasma in a manner similar to that for reagent A, and when this was used it was found that patients with classic haemophilia reacted in the same way as normal subjects.

The authors consider their test to be more specific than other tests for the diagnosis of haemophilia. They note that other workers have found more than one type of deficiency in apparently true haemophilia.

John F. Loutit

1633. **The Pathogenesis of Essential Thrombocytopenia.** (Die Pathogenese der essentiellen Thrombozytopenie)
P. MIESCHER, A. VANNOTTI, S. CRUCHAUD, and G. HEMMELER. *Experimental Medicine and Surgery* [*Exp. Med. Surg.*] **10**, 265–286, 1952. 12 figs., bibliography.

The observation that children born of mothers with chronic thrombocytopenic purpura themselves have thrombocytopenia for 1 to 3 months after birth has led to the assumption that some kind of antibody must be the cause, it being known that small blocking antibodies can pass through the placental filter. This theory is supported by the observation that transfusion of blood from patients with chronic thrombocytopenia into normal persons results in thrombocytopenia in the recipient for some days. The thrombocytopenic factor is not species-specific, and the patient's serum produces thrombocytopenia when injected, even intradermally, into rabbits and guinea-pigs. If the serum is given in sufficient dosage, fatal anaphylactic shock may occur in rabbits, but can be prevented by the previous administra-

tion of antihistamines. The same dose of serum given to previously splenectomized animals, however, does not cause shock, and the resultant thrombocytopenia is more transient and less severe than in intact animals.

In 2 out of 4 cases of chronic idiopathic thrombocytopenia studied by the authors, the patient's serum agglutinated normal platelets *in vitro*, the active substance being removed from the serum in the process. In one case the patient's serum caused phagocytosis of platelets by neutrophil granulocytes *in vitro*. It is concluded that chronic thrombocytopenic purpura is due to autosensitization, the organism becoming sensitized to its own thrombocytes. *A. Piney*

NEOPLASTIC DISEASES

1634. **Plasma Cell Myeloma**
G. C. MEACHAM. *Annals of Internal Medicine* [*Ann. intern. Med.*] **38**, 1035–1047, May, 1953. 4 figs., 16 refs.

Details are presented of 51 cases of plasma-cell myeloma studied at the University Hospitals of Cleveland, Ohio, since 1933. There were 22 female and 29 male patients, and 42 (82·3%) of them were 50 years of age and over. Anaemia was almost invariably present, and was macrocytic in 22 of the 29 patients in whom the mean corpuscular volume was determined. In 48 of 50 cases examined radiologically osseous abnormalities were found, diffuse osteoporosis being a common finding. The diagnosis depends on the finding of an excessive number of immature plasma cells in marrow smears. Hyperglobulinaemia, Bence Jones proteinuria, and a raised ionized calcium level in the serum were common, the last two findings being usually associated with renal insufficiency. With regard to treatment, radiotherapy resulted in temporary relief of local lesions, and administration of urethane produced marked symptomatic improvement without influencing the course of the disease. ACTH and cortisone were valueless. The period of survival was less than 2 years in most cases, but 2 patients lived 3½ and 5½ years respectively.
J. L. Markson

1635. **The Myeloproliferative Disorders. With Special Reference to Myelofibrosis**
M. S. R. HUTT, J. L. PINNIGER, and G. WETHERLEY-MEIN. *Blood* [*Blood*] **8**, 295–314, April, 1953. 22 figs., 14 refs.

The authors set out to show the close relationship between fibrosis of the bone marrow and various leukaemoid blood diseases. From St. Thomas's Hospital, London, 10 cases of myeloproliferative disorders are described, 6 of them with post-mortem findings. These include one classic case of myeloid leukaemia and one of myelofibrosis, the other 8 being cases with varying clinical and haematological features predominantly suggestive of myeloid leukaemia, myelofibrosis, or polycythaemia. A special study was made of marrow biopsy specimens from the sternum, iliac crest, and ribs, and sections were specially stained for reticulin. The liver, spleen, adrenal glands, kidneys, and lymph nodes were also examined, when available, for evidence of haematopoietic elements. The cases were specially selected to support the view that myelofibrosis, myeloid leukaemia, megakaryocytic myelosis, and polycythaemia are related processes.

It was possible to demonstrate more than one line of development of neoplastic cells in individual cases, and the authors conclude that this is evidence that these proliferative disorders of the haematopoietic system, including myelofibrosis, are closely related neoplastic processes involving multipotential primitive mesenchymal cells. They suggest that extramedullary haematopoiesis in myelofibrosis is not compensatory, but is a further manifestation of the mesenchymal overgrowth.
Mary D. Smith

1636. **Remittent Generalized Lymphoreticulosis.** (Lympho-réticulose généralisée rémittente)
R. CLÉMENT, B. DUPERRAT, J. GERBEAUX, A. COMBES-HAMELLE, and G. BOUVEAU. *Presse médicale* [*Presse méd.*] **61**, 585–588, April 22, 1953. 10 figs., 24 refs.

The authors describe in some detail an acute febrile disease, characterized by enlargement of the spleen and lymph nodes, a rash, and mononucleosis of the blood and bone marrow, which they have encountered in 6 boys between the ages of 2 and 10 years. The onset is abrupt, with a rise of temperature to 39° or 40° C. (102° or 104° F.) or even higher, the early signs being those of tonsillitis, soon followed by a rash which may be scarlatiniform or resemble that of measles. After the first 2 days considerable swelling of the lymph nodes in all areas and enlargement of the spleen occur, and there may be pain in the joints (2 out of 6 cases). All signs and symptoms disappear within a week or two, only to recur after a variable time, one child having as many as 7 attacks over a period of several months. With each attack the patient may be severely ill, becoming dehydrated and cachectic, delirious, and at times unconscious. Neck rigidity may be present, and petechiae appear everywhere. On lumbar puncture the findings are normal and there is no evidence of infection. The blood and bone marrow show a moderate mononucleosis and monocytosis.

Biopsy of a cervical lymph node shows a histological picture liable at first to be mistaken for that of lymphogranuloma; however, the architecture of the gland is fairly normal, although no normal germ-centres can be seen and the follicles show confluence.

The case is described in detail of a child of 10 who had repeated attacks, gradually diminishing in severity, at intervals over a period of 4 months, after which he recovered completely and has remained fit during a 6-year follow-up period. The authors emphasize that the diagnosis in such cases cannot be made on clinical, haematological, biochemical, or radiological grounds, histological examination being necessary to differentiate the condition at an early stage from leukaemia and other acute affections of the reticulo-endothelial system. There are a number of good diagrams and photomicrographs. *L. Michaelis*

Respiratory System

1637. **Solitary Pleural Mesotheliomas**
H. W. BENOIT and L. V. ACKERMAN. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **25**, 346–357, April, 1953. 4 figs., 12 refs.

The authors refer to the confusion which exists regarding the origin and classification of primary pleural tumours, and attribute to Stout and Murray (*Arch. Path.* (*Chicago*). 1942, **34**, 951) the most satisfactory classification so far. This consists in grouping the solitary tumours, which may be benign or of low-grade malignancy, as " solitary " mesotheliomata, and the diffuse and spreading tumours, which are of high-grade malignancy, as " diffuse " mesotheliomata. The histology is described. The first group may include tumours which have previously been described as fibroma, fibrosarcoma, sarcoma, myxosarcoma, leiomyosarcoma, and endothelioma.

Solitary mesothelioma is rare and the diffuse variety even more rare. However, the authors are satisfied that they have found 11 cases of solitary mesothelioma in the literature, which, with the 6 new personal cases now described from the Washington University School of Medicine, St. Louis, form the basis of this study. Detailed histories of the 6 cases, illustrated by radiographs and photomicrographs of histological preparations, are given. It is emphasized that solitary mesotheliomata are usually benign. Diagnosis may be difficult, as symptoms are often slight until the tumour has reached a considerable size. The most usual symptoms are chest pain, cough, and dyspnoea, and a prominent clinical feature may be clubbing of the digits with arthralgia and arthropathy of the knee, wrist, and elbow joints. All signs and symptoms may disappear in a dramatic way after operative removal of the tumour, as occurred in 3 of the authors' 6 cases. *Bryan P. Moore*

1638. **Tracheal Resection and Replacement with a Prosthesis**
R. L. CRAIG, G. W. HOLMES, and E. J. SHABART. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **25**, 384–396, April, 1953. 8 figs., 18 refs.

The problem of successful resection of portions of the trachea and larger bronchi has up to the present found no satisfactory solution. In a review of the literature the authors show that many workers have demonstrated that window defects can usually be satisfactorily repaired by a variety of means. Gebauer in particular has used dermal grafts reinforced with stainless steel wire, but his preference is for direct end-to-end anastomosis wherever this is possible. The real problem remains with cuff or segmental resections of the trachea in cases in which direct anastomosis is not possible. A variety of tissues and materials such as plastic tubes, wire mesh, and reinforced fascia have been used, but all suffer from the same defects and disadvantages, namely: (1) the difficulty of producing and maintaining an airtight junction; (2) the difficulty experienced by the patient in expelling secretions from the distal bronchial tree past the inert segment of trachea—resulting in a high incidence of acute and chronic lung infection; (3) the great liability to the development of stenosis at the site of the junction; and (4) the grave risk of the prosthesis becoming loose and impacting in the bronchial tree.

In experiments on dogs carried out at the Northwestern University Medical School, Chicago, the authors have attempted to carry the solution of the problem one stage farther by the use of a specially prepared polythene tube made from fused polythene sheeting reinforced with wire. The advantages of this type of tube over other polythene tubes is that it is flexible and capable of being sutured carefully in place without risk of the sutures cutting through; also it can be readily prepared in different sizes and thus the attainment of an airtight fit is possible. In the experiments described both extratracheal and endotracheal application of the prosthesis was investigated. In the former case stenosis resulted in all the animals which survived the procedure. With endotracheal application stenosis was less common, but respiratory infections and obstruction from a slipped prosthesis were not eliminated. The use of the method in tracheal resection for a tumour in one human patient is described, but the patient died on the fifth postoperative day from atelectasis and pulmonary infection. Because of the fact that tracheal regeneration does not occur, the authors doubt whether any type of prosthesis will ever prove satisfactory in the trachea, but suggest that the tube used in these experiments might be used in the repair of the oesophagus or large blood vessels. *W. P. Cleland*

LUNGS AND BRONCHI

1639. **Biopsy Techniques in the Diagnosis of Intrathoracic Lesions, including Lung Biopsy, Mediastinal Biopsy and Resection of the Deep Cervical Fat Pad and its Contained Nodes. Report of 12 Illustrative Cases**
C. F. STOREY and B. M. REYNOLDS. *Diseases of the Chest* [*Dis. Chest*] **23**, 357–382, April, 1953. 12 figs., 10 refs.

The correct treatment of intrathoracic lesions depends on accurate histological diagnosis. In certain cases where bronchoscopic and oesophagoscopic findings are negative, other biopsy techniques are available, but do not appear to have been generally employed. These are: (1) resection of the deep cervical (supraclavicular) fat pad and its associated nodes; (2) mediastinal biopsy at open thoracotomy; and (3) lung biopsy at open thoracotomy.

The authors have used these methods in an appreciable number of cases at the U.S. Naval Hospital, St. Albans,

Long Island, New York, and have been able to establish a definite diagnosis in nearly every instance. There has been no associated mortality, and only minimal morbidity.

To illustrate these methods of treatment 12 cases are reported in detail, with radiographs and photomicrographs; they include cases of mediastinal Hodgkin's disease, sarcoidosis, eosinophilic granuloma of lung, mediastinal tuberculoma, and carcinoma of lung (primary and secondary).

A plea is made for the greater use of these methods in the investigation of obscure chest lesions.

F. J. Sambrook Gowar

1640. **Metastasizing Bronchial Adenomas**

R. P. McBurney, J. W. Kirklin, and L. B. Woolner. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **96**, 482–492, April, 1953. 9 figs., 11 refs.

A study of 111 cases of bronchial adenoma diagnosed and verified histologically at the Mayo Clinic since 1937, together with a review of 700 cases in the literature, has shown that approximately 10% metastasize either to the regional nodes or to distant organs. Nine of these cases are reported in detail, and the authors find that the cylindromatous variety is three times more likely to metastasize than the carcinoid type.

G. J. Cunningham

1641. **Endoscopic Diagnosis of Early Bronchial Carcinoma**

F. Eeman. *Journal of Laryngology and Otology* [*J. Laryng.*] **67**, 266–276, May, 1953.

The increase, not only relative but also real, observed in the incidence of carcinoma of the lung in recent years has made early diagnosis a matter of urgency. This can best be achieved by the early use of radiology, bronchoscopy, bronchography, endoscopic biopsy, and cytological examination.

A lateral radiograph often demonstrates the sharply defined triangular shadow with a peripheral base and a bronchial apex denoting atelectasis which may be missed in an antero-posterior film, and a lateral radiograph should therefore always be obtained. Tomography may also be helpful in some cases, but the location and nature of the lesion can only be accurately revealed by bronchoscopy or bronchography. As bronchography spoils the field for subsequent bronchoscopy, the latter should be performed first, since even small lesions, because of their tendency to grow always towards the centre, do not easily pass unnoticed by the trained eye. A pedunculated tumour may be visible at the orifice of the upper-lobe bronchus only for a fraction of a second during coughing. Endoscopic biopsy is the most satisfactory method of diagnosis. The taking of a biopsy specimen of a flat tumour is sometimes difficult, and several forceps are necessary, all of which must have cutting edges. Special forceps fitted with lenses between the jaws are helpful for deep-seated biopsies. Many types of forceps, including curved, elastic forceps which are directed under observation through a right-angle telescope, have been suggested, but none entirely solves the problem. The biopsy specimen having been obtained, there still remains the difficulty of interpretation by the pathologist, and the author emphasizes the risk of being too ready or too optimistic in accepting a negative finding. In doubtful cases cytodiagnosis should be used, material for this being easily obtained from sputum, or by swab or aspiration. The drawbacks of this procedure are that it is time-consuming for the pathologist, doubtful findings are more frequent than with biopsy, and a negative finding is of little or no value. Nevertheless, cytological examination should be resorted to in every doubtful case.

C. Eisinger

1642. **The Correlation of Carcinoma and Congenital Cystic Emphysema of the Lungs. Report of Ten Cases**

E. Korol. *Diseases of the Chest* [*Dis. Chest*] **23**, 403–411, April, 1953. 4 figs., 1 ref.

Ten cases of carcinoma of the lung developing in middle-aged war veterans with congenital cystic emphysema of the lung are reported. Seven were found in a follow-up study of 40 cases of congenital cystic emphysema over a period of 13 years. In 60 cases of diffuse pulmonary emphysema complicating bronchial asthma and lung infections followed for the same length of time no bronchial carcinoma developed.

A review of the literature disclosed 45 cases (9%) of lung cancer among 500 persons of all age groups with congenital cystic emphysema. The incidence is 1·5% in autopsies of adults in the general population. In cystic emphysema, carcinoma occurs at an earlier age and with a significantly greater frequency than in the general population.—[Author's summary.]

1643. **The Factor of Infection in Chronic Bronchitis**

C. H. Stuart-Harris, M. Pownall, C. M. Scothorne, and Z. Franks. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **22**, 121–132, April, 1953. 2 figs., 11 refs.

The authors investigated the bacterial flora of the sputum of 113 patients with chronic bronchitis (90 males and 23 females) admitted to hospital in Sheffield between the years 1949 and 1952. *Streptococcus pneumoniae* was found in 50·5% of specimens, *Haemophilus influenzae* in 15·0%, and *Staphylococcus pyogenes* in 11·6%. In the case of the *Haemophilus* organisms selective media were not employed for isolation, and it is considered that the actual percentage was in fact somewhat higher. Evidence of infection by influenza virus Types A and B was found chiefly in cases of acute exacerbation of the chronic bronchitis.

It is concluded from a consideration of the types of pneumococci present in the sputum that this organism is most probably derived autogenously from the nasopharynx. The resemblance between the sputum in chronic bronchitis and in bronchiectasis, in spite of the gross anatomical lesions in the latter disease, is pointed out, as is the effect of antibiotics in reducing the quantity and altering the quality of the sputum. The final conclusion is drawn that in chronic bronchitis there is a failure of the defence mechanisms of the lower respiratory tract against invasion by nasopharyngeal organisms.

John M. Talbot

Otorhinolaryngology

1644. **Cardiac Arrest from the Otolaryngologist's Viewpoint**
R. M. Hosler. *Archives of Otolaryngology* [*Arch. Otolaryng. (Chicago)*] **57**, 371–377, April, 1953. 6 refs.

In the opinion of the author, who writes from Cleveland, Ohio, cardiac arrest is a relatively frequent complication during otolaryngological operations, yet otolaryngologists, as a group, are not fully prepared to deal with it. While reliable figures are not available, he believes that cardiac arrest occurs more frequently now than in the past; he quotes " a conservative figure that is often used ", namely, an average of 5 cases of cardiac arrest every year in an active 700-bed hospital.

Discussing some of the factors contributing to cardiac arrest, he points out that the "accepted figure" for mortality from ether anaesthesia in skilled hands is 1 in 16,000, and that chloroform is 25 times more toxic to the myocardium than ether. Procaine and cocaine have a depressant effect on the heart and can stimulate the brain to convulsions. If the rate of absorption of a local analgesic exceeds the rate of detoxification, the concentration in the blood mounts. A drug injected into a mucous membrane is absorbed almost as quickly as if injected into a vein. Adrenaline causes the oxidation rate of all tissues to increase, and this, in an irritable heart or one depressed by the anaesthetic, may result in fibrillation. A temporary overdose—for example, of procaine—causes vasodilatation, relaxation of the heart muscle, and bradycardia; the coronary pressure becomes ineffective and cardiac arrest supervenes.

Resuscitation in cases of cardiac arrest is carried out in two steps: (1) re-establishing oxygenation of the blood, and (2) restoring the heart beat. One of the gravest hazards in otolaryngological operations is, in the author's view, the sitting position of the patient under local analgesia. Hence the first step is to place the patient " in such a position that he is practically standing on his head "; this has the effect of giving him a transfusion of 600 to 700 ml. of whole blood which has been stagnant in the dependent parts. A tube is placed in the trachea and 100% oxygen is delivered to the lungs under positive pressure. The chest is opened in the fifth left intercostal space and the heart and intact pericardium are squeezed upwards against the sternum. If the heart does not respond rhythmically, a rib retractor is inserted, the pericardium opened, and massage resumed. The heart may be in standstill or in ventricular fibrillation. The heart in standstill may start to beat again with massage alone; if, however, after a period of adequate massage the heart does not start, 4 or 5 ml. of a solution of 1 in 10,000 adrenaline is injected into the right ventricle. In difficult cases a mechanical respirator is of help. To overcome fibrillation an electric shock may be needed as well as massage, and an injection into the chamber of a solution of 1% procaine hydrochloride in addition is helpful.

The author concludes by suggesting that all surgeons should be prepared for the eventuality of cardiac arrest and for carrying out these resuscitative measures.

F. W. Watkyn-Thomas

NOSE

1645. **Irradiation of Malignant Nasopharyngeal Tumours.** (К клинике и рентгенотерапии злокачественных опухолей носоглотки)
Y. F. Levin and D. E. Rozengauz. *Вестник Оториноларингологии* [*Vestn. Oto-rino-laring.*] 45–49, No. 1, Jan.–Feb., 1953.

Over a number of years 49 cases of malignant nasopharyngeal tumour have been observed at the Ukrainian Röntgen, Radiological, and Oncological Institute, Kharkov, of which 25 were carcinoma, 16 sarcoma, and 8 lympho-epithelioma. In 5 of the cases of sarcoma the patients were aged between 10 and 12 years, and in 11 cases an incorrect diagnosis of tuberculous adenopathy of the neck had been made before admission.

The first signs to appear were enlarged cervical nodes, nasal obstruction, and the sensation of a foreign body in the pharynx. In some circumscribed tumours of the nasopharynx symptoms were completely absent, and in others the enlarged nodes were the only sign. Even biopsy of the nodes did not always provide a certain diagnosis. The symptoms were most marked in tumours arising low down and anteriorly, while invasion of the soft palate caused difficulty in breathing, changes in the voice, and, less commonly, epistaxis and dysphagia. Blood-stained purulent discharge was a later sign and occurred in cases of both carcinoma and sarcoma. Unilateral deafness and tinnitus occurred when the tumour was situated laterally.

Extension of the growth to the orbit and base of the skull was common, orbital symptoms (tension, severe pain, proptosis with outward displacement, and limitation of movement), trigeminal nerve lesions, and loss of visual acuity being observed in 6 out of 49 patients; in 9 cases the tumour had extended along the base of the skull, paralysis of the 6th cranial nerve and trigeminal neuralgia occurring in this group, while anaesthesia and loss of corneal reflex occurred later. Lesions of the motor fibres of the 5th nerve caused deviation of the jaw to the side when the mouth was opened. Severe pain in the second and, to a lesser extent, the third division of the trigeminal nerve, with trismus, was noted in one case involving the pterygopalatine fossa. In 2 cases there were lesions of the jugular foramen, with paralysis of the soft palate, vocal cord, and loss of the glottic reflex. Lesions of the cervical sympathetic nerves were also seen. Some tumours at the base of the skull extended through the superior orbital fissure into the orbit. Carcinoma showed the most marked tendency to extend along the base of the

skull, and sarcoma to extend into the orbit. In only 11 patients was the disease limited to the nasopharynx, and the cervical nodes were invaded in 30 cases (60%).

Biopsy was performed on 41 out of the 49 tumours; of 8 cases in which biopsy of the lymph nodes only was made, 5 were diagnosed as carcinoma and 3 sarcoma. Following biopsy of the primary tumour in 33 cases histological examination gave the following results: differentiated squamous-cell carcinoma 8 cases, undifferentiated squamous-cell carcinoma 5, transitional-cell carcinoma 1, adenocarcinoma 1, round-cell sarcoma 5, lymphosarcoma 3, sarcoma 2, and lympho-epithelioma 8. In 4 out of 25 cases of carcinoma, 3 out of 16 of sarcoma, and 2 out of 8 of lympho-epithelioma distant metastases were observed.

All cases were treated by prolonged fractional irradiation (dosage 3,000 to 6,000 r). One patient with carcinoma was free from recurrence after 5 years, and 2 after 2 years; 3 patients with sarcoma have survived 12 to 18 months. In cases of lympho-epithelioma the immediate results were good even in the presence of bilaterally affected cervical nodes, but metastases developed in 3 to 4 months, and in 2 patients local recurrence appeared.

Stephen Suggit

1646. **Streptokinase and Streptodornase in Chronic Maxillary Sinusitis.** (Streptokinase, streptodornase et sinusites maxillaires chroniques)
P. GUNS and E. DOYEN. *Annales d'oto-laryngologie* [*Ann. Oto-laryng.* (*Paris*)] **70**, 21–25, 1953. 1 fig., 12 refs.

The authors have treated 3 cases of chronic purulent maxillary sinusitis with injections into the sinus of streptokinase and streptodornase, enzymes of streptococcal origin which are capable of dissolving fibrin and reducing the viscosity of exudates. In 2 of the 3 cases there was marked evidence of local irritation, suggesting that the nasal mucosa is sensitive to the enzymes, which may therefore impair the integrity of ciliary motion. Moreover, such irritation causes a proliferation of basal cells with excessive secretion of mucus, on which the two enzymes have no effect. It is therefore concluded that the only indication for the intranasal use of these enzymes is in cases of acute purulent sinusitis in which the contents of the affected sinus are so viscous as to prevent their evacuation by simple lavage—repeated lavage followed by instillation of antibiotics being the treatment of choice in such cases.

E. D. Dalziel Dickson

1647. **Extract of *Aspergillus fumigatus* Applied Locally in the Treatment of Rhinitis. Its Use by Proetz's Method in the Treatment of Sinusitis.** (L'extrait d'*Aspergillus fumigatus* en application locale dans le traitement des rhinites. Son emploi par la méthode de Proetz dans le traitement des sinusites)
J. RICHIER and J. MERCIER. *Annales d'oto-laryngologie* [*Ann. Oto-laryng.* (*Paris*)] **70**, 5–20, 1953. 7 figs.

The authors describe their method of treating rhinitis and certain forms of sinusitis by the Proetz displacement technique with a solution of the antibiotic aspergillin, which is extracted from cultures of *Aspergillus fumigatus*. The indications are discussed, and the technique of displacement is described in detail. Allergic rhinitis, acute sinusitis, and multiple polyposis are contraindications to this form of therapy.

Their results are given as follows. (1) Of 840 cases of infection of the posterior nasal sinuses treated, 788 were cured after 4 to 8 attendances. (2) Of 210 cases of infection of the ethmoidal cells alone (in some of which vaccines were also used), 202 were cured. (3) Of 315 cases of ethmoiditis with associated maxillary sinusitis, 71 were cured by the aspergillin displacement method alone, 96 by displacement combined with vaccine therapy, and 130 by displacement combined with antral puncture and direct instillation of aspergillin, only 18 cases remaining in which these methods of treatment failed. (4) Of 31 cases of simple ethmoiditis in children, 26 were cured, while of 41 in which there was also unilateral maxillary sinusitis (and in which vaccine therapy was also used), 32 were cured.

E. D. Dalziel Dickson

EAR

1648. **Variations due to Age in the Bone Conduction Threshold of Hearing.** (Возрастные изменения порогов слышимости при костной проводимости)
N. V. TIMOFEEV and K. P. VOKRYVALOVA. *Вестник Ото-рино-ларингологии* [*Vestn. Oto-rino-laring.*] 31–33, No. 1, Jan.–Feb., 1953. 2 figs.

The threshold of bone conduction of 125 subjects (36 men and 89 women) was determined audiometrically, an electromagnetic bone conductor being used in 80 cases and a piezoelectric bone conductor in the remaining 45. The subjects were instructed to hold the conductor over the point of the mastoid process at which hearing was best; this point was usually over the antrum. The threshold was estimated by decreasing the stimulus from an audible to an inaudible level, and then reversing the process. The frequencies tested extended from 100 to 1,200 cycles per second (c.p.s.) and the stimulus was maintained for 5 to 8 seconds, followed by a pause of 2 to 4 seconds.

The age groups 7–13, 14–19, 20–29, and 30–39 years all showed similar thresholds and were used as the base line. In the age groups 40–49 and 50–59 the thresholds were also nearly alike and are shown together in the two graphs reproduced. A considerable rise of threshold was noted in the 60–69 age group, and an even greater rise in the 70–79 age group, the rise of threshold increasing relatively towards the high frequencies, and rising sharply at 8,000 c.p.s. The readings obtained with the electromagnetic and piezoelectric conductors (shown in separate graphs) showed little difference.

Stephen Suggit

1649. **Pathogenesis and Histopathology of Chronic Adhesive Otitis**
L. OJALA. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **57**, 378–401, April, 1953. 9 figs., 28 refs.

Urogenital System

1650. **On the Artificial Kidney—XXII. Dialytic Treatment in Four Selected Cases of Acute Glomerulonephritis. A Contribution to the Question of the Need for Dialysis in Rational Renal Therapy.** [In English]
N. ALWALL, A. LUNDERQUIST, and A. TORNBERG. *Acta medica Scandinavica* [*Acta med. scand.*] **145**, 175–180, April 30, 1953. 2 figs., 8 refs.

This is a further report from the Medical Clinic of the University of Lund, Sweden, on the effect of dialysis in renal failure, in which 4 selected cases of acute glomerulonephritis so treated are described. One patient, a woman aged 39, recovered, after conservative treatment with maintenance of electrolyte balance, high-calorie diet (oil and glucose), and fluid replenishment had failed to stimulate diuresis, when the artificial kidney (Alwall's modification) was used on the 7th day of anuria; she was anuric or oliguric for 14 days in all. Another patient, a woman aged 51, who was given dialysis after 11 days of anuria, also survived, anuria or oliguria in this case lasting for 21 days. The 2 other patients, men aged 59 and 26 respectively, died. The elder of these passed 211 ml. of urine in 38 days, the younger 80 ml. in 21 days, the latter living for another 20 days with complete anuria. These 2 patients had treatment with the artificial kidney on 2 and 4 occasions respectively. The immediate result was dramatic; the unconscious patients became wide awake and mentally alert, and cooperated in their treatment by taking the oil–glucose diet, but their renal failure remained unaffected. In both of them kidney function had been abolished by diffuse glomerulonephritis with fibrosis and hyalinosis.

The authors consider that the use of dialytic treatment should depend on the rate of protein destruction as reflected in the fluctuation of the non-protein nitrogen level of the serum, which differs widely in each individual case.

L. H. Worth

1651. **Innate Functional Defects of the Renal Tubules, with Particular Reference to the Fanconi Syndrome. Cases with Retinitis Pigmentosa**
W. P. U. JACKSON and G. C. LINDER. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **22**, 133–156, April, 1953. 5 figs., bibliography.

Current knowledge of the various syndromes resulting from defects of renal tubular function is reviewed, with special reference to 4 cases investigated at the University of Capetown. The best-known syndrome is that named after Fanconi, which is characterized by vitamin-D resistant rickets with a low serum phosphorus level, glycosuria, aminoaciduria, albuminuria, and acidosis.

The first patient, a deaf-mute boy aged 10 years, was physically and mentally retarded and, when first seen, had retinal degeneration with pigmentation and rickets. The serum phosphorus and calcium levels were low, while the phosphatase level was raised. This patient had a slight but continuous acidosis and glycosuria. The same type of retinal degeneration was found in the patient's sister, who was also a deaf-mute, but there was no evidence of rickets. The only abnormality in the serum of this second patient was a slight increase in both the phosphatase and cholesterol levels. Both patients had albuminuria, and the concentration of the urine was low in both. [The results of water restriction on urinary concentration are not reported.] In the first patient the glomerular filtration rate and PAH clearance were low, while poor excretion of phenolsulphonphthalein in both indicated tubular defect. In both there was a small but definite increase in urinary excretion of organic acids and a surprisingly low excretion of calcium. The clearance of phosphate in the first patient was very high. In the authors' view these findings indicated that both glomerular and tubular functions were impaired, more so in the first patient than in the second. The administration of a daily dose of 400,000 units of vitamin D resulted in an increase in the serum phosphorus and calcium levels in the first patient, with an improvement in the rickets and gain in body weight.

The clinical picture in the third patient in this series was one of retinitis pigmentosa, rickets, glycosuria, osteoporosis, and infantilism, with persistent polyuria. Excretion of organic acids and of amino-acids was much increased. The serum phosphorus level was usually low. The fourth patient, a sister of the third, also had retinitis pigmentosa, and almost certainly had renal tubular deficiency as well.

The mechanism of the syndrome and of various allied disorders is discussed at length. [The reader is advised to consult the original for this interesting discussion.]

G. Loewi

1652. **Bright's Disease. An Attempt at a Statistical Assessment of the Classification Proposed by Ellis**
J. B. ENTICKNAP and C. L. JOINER. *British Medical Journal* [*Brit. med. J.*] **1**, 1016–1020, May 9, 1953. 7 figs., 11 refs.

The clinical and histological features of 127 fatal cases of Bright's disease from the necropsy records of Guy's Hospital, London, for the period 1931–51 were re-examined by the authors, and clinical and pathological diagnoses made independently in each case according to the classification proposed by Ellis (*Lancet*, 1942, **1**, 1, 34, and 72). Agreement between the two diagnoses was reached in a significant proportion of cases in all groups, although the degree of agreement varied, being less close for the chronic inflammatory conditions than for any other of the major forms of renal disease. Considerable overlapping was discovered between nephritis of Types I and II, there being 18 cases in which one type was diagnosed clinically and the other

pathologically, and in which agreement could not be reached on re-examination; full details are given of 7 of these. Histologically, while the distinctive pictures described by Ellis did occur in pure form, in many cases features of several of these pictures existed side by side in the same kidney. In particular, subendothelial hyalinization of the capillaries—characteristic of the Type-II lesion—was encountered in ischaemic and other kidneys unassociated with a history of nephritis. The conclusion is drawn that until a satisfactory classification based on aetiology becomes available there is little reason to depart from the time-honoured subdivision of clinical nephritis into acute, subacute, and chronic forms.

L. H. Worth

1653. **Polymyxin B in Pyelonephritis: Observations on the Safety of the Drug and on Its Influence on the Renal Infection**

J. HOPPER, E. JAWETZ, and F. HINMAN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **225**, 402–409, April, 1953. 14 refs.

1654. **Relationship of Colloids to the Surface Tension of Urine**

R. A. RAVICH. *Science* [*Science*] **117**, 561–563, May 22, 1953. 1 fig., 4 refs.

Local conditions, sometimes transitory, are important factors in the aetiology of urinary lithiasis in a large proportion of cases; but in addition to these there are various constitutional metabolic conditions which may contribute to the production of calculi, especially in cases of recurrent stone formation. Interest in this aspect of urinary lithiasis has recently been renewed by the work of Butt (*J. Urol.*, 1952, **67**, 450; *Abstracts of World Medicine*, 1952, **12**, 346) who, following the suggestion made by Ebstein in 1884 that the urinary crystalloids remain in the dissolved state through the protective action of the colloids, has shown that the number of urinary colloid particles visible under the ultramicroscope may be increased by the administration of hyaluronidase, and that by this means the formation of new stones may be delayed or prevented (*Calif. Med.*, 1952, **76**, 123; *Abstracts of World Medicine*, 1952, **12**, 251). The protective effect of the colloids was attributed by Butt to their influence upon the surface tension of the urine.

In a series of investigations here reported the author has confirmed the finding that specimens of urine containing a large number of colloid particles generally have a low surface tension and vice versa. But in a significant number of specimens examined the surface tension was high despite the presence of large numbers of colloid particles, which suggests that the surface tension is not necessarily dependent on colloid activity but that both are determined by some other factor as yet not understood. The protective action of hyaluronidase may thus have been due to the higher degree of colloid activity or to the reduced surface tension observed in the urine of treated patients, or possibly to this unknown factor. Further investigations into the action of hyaluronidase and on the factors influencing colloid activity and surface tension of urine are therefore desirable.

James Kemble

1655. **Bladder Tumor Recurrence in the Urethra: a Warning**

J. H. KIEFER. *Journal of Urology* [*J. Urol. (Baltimore)*] **69**, 652–656, May, 1953. 6 refs.

The author reports 5 cases of implantation of a bladder tumour into the posterior urethra. In all the cases the original tumour had been dealt with transurethrally by a resection instrument, and in 4 of them transurethral resection of the bladder neck had been performed at the same time. The recurrence was always found at the distal edge of the resected area. In 3 of the cases the histological diagnosis was carcinoma, in one papilloma, and in the other a negative finding was reported. These 5 cases, which were seen at the St. Joseph Hospital, Chicago, have all occurred in the last 6 years, the author stating that he has had no similar case in the previous 10 years. He is convinced that resection of the bladder neck at the time of resection of the tumour is an important aetiological factor, and recommends that the two precedures should no longer be carried out at the same operation. He considers that no re-examination in a case of neoplasm of the bladder is complete without a posterior urethroscopy as well as a cystoscopy.

Victor W. Dix

1656. **The Effect of Banthine in the Treatment of Genito-urinary Disorders**

J. W. DRAPER, S. WOLF, J. F. MURPHY, and H. KRAVETZ. *Journal of Urology* [*J. Urol. (Baltimore)*] **69**, 632–640, May, 1953. 5 figs., 9 refs.

The authors, at Bellevue Hospital, New York, have investigated the effect of "banthine" (methantheline) bromide on the urinary bladder in 74 patients with various bladder disorders and in 17 subjects with a normal bladder, the drug being administered by mouth in single doses of 100 to 150 mg. or in repeated doses of 50 to 100 mg. 4 times a day. The effect of intramuscular injections of 25 to 50 mg. was also observed.

It was found that where the bladder capacity was already more than 250 ml. oral administration of single doses of banthine might increase it by 100 ml. With smaller bladder capacity the drug had a correspondingly greater effect. Similar results were obtained with intramuscular injections of single and of repeated doses. The capacity of 4 out of 10 normal bladders was increased by 20 to 47%, but the increase in capacity of the other normal bladders was insignificant. In each of 6 patients with chronic cystitis the bladder capacity was doubled while banthine was being taken. The drug was also found to have an inhibitory effect on the hypertonus of the bladder induced by drugs stimulating the parasympathetic system.

The authors conclude from their investigation that banthine may be of use in cases of renal colic.

Victor W. Dix

1657. **Electrocystography: a Study of Bladder Contractions Measured by Difference of Electropotential**

G. S. SLATER. *Journal of Urology* [*J. Urol. (Baltimore)*] **69**, 626–631, May, 1953. 8 figs., 9 refs.

Endocrinology

THYROID GLAND

1658. **Prognosis of Hyperthyroidism Treated by Antithyroid Drugs**
D. H. SOLOMON, J. C. BECK, W. P. VANDERLAAN, and E. B. ASTWOOD. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **152**, 201–205, May 16, 1953. 2 figs.

The authors have studied 101 hyperthyroid patients for a period of at least 4 years following treatment with antithyroid drugs at the Peter Bent Brigham and New England Center Hospitals, Boston, Massachusetts. Of this number, 24 (23·7%) had a relapse within 3 months, 21 (20·8%) had a recurrence in 3 to 48 months, and 56 (55·5%) were euthyroid after 4 years. Second and third courses of therapy were given to 33 of the patients in whom a relapse had occurred; the remission rate was lower in this group, but the total number of patients with a prolonged remission rose to 71 (70·3% of the whole series).

Any clinical characteristics which might indicate the probability of a prolonged remission were sought, but a decrease in goitre size during therapy was the only factor correlated significantly with a good ultimate result. Primary hyperthyroidism and a small diffuse goitre are also considered to favour the occurrence of a prolonged remission. The thyroid was of normal size in 46 (75%) of the 61 patients in remission after 4 years in whom this was determined, and evidence is presented that hyperplasia of the thyroid disappears after prolonged remission.

F. W. Chattaway

1659. **The Functional Condition of the Central Nervous System in Thyrotoxic Patients.** (К вопросу о функциональном состоянии центральной нервной системы у больных тиреотоксикозом)
M. G. AMIRAGOVA. *Клиническая Медицина* [*Klin. Med.* (*Mosk.*)] **31**, 46–55, April, 1953. 5 figs., 4 refs.

The functional condition of the central nervous system was compared in normal subjects and in 40 thyrotoxic patients by investigation of the vasomotor reflexes by plethysmography; the responses to exteroceptive stimuli (heat and cold) and to interoceptive stimuli (dilatation of the rectum by a rubber bulb connected to a manometer) showed marked differences as between normal subjects and thyrotoxic patients. The left arm was placed in a plethysmograph, while the right forearm was used for application of the thermal stimuli. The tests were repeated several times in each case, 5 to 20 tests being made before operation, 3 to 5 a fortnight later, and others up to 4 months after thyroidectomy.

The patients fell into two groups according to response: those with heightened reactivity, and those who were inert or gave paradoxical responses. The threshold of response to increased pressure in the rectum in normal persons was 60 mm. Hg, which caused vasodilatation, whereas in some of the thyrotoxic subjects a pressure of 30 to 40 mm. Hg was sufficient in some cases to provoke vasodilatation, in others vasoconstriction. In the hyperreactive group, successive stimuli often provoked increased responses. Sometimes the response took on a wave-like character which persisted for several seconds after withdrawal of the stimulus. In the inert group, the threshold of response was higher, and often no response was produced by the thermal stimuli; the response to stimuli from the interoceptive reflexes was more often paradoxical. The stimuli were preceded by words such as, " I am going to give you something cold," thus producing a conditioned reflex which in normal and hyperreactive thyrotoxic patients was sufficient to induce a vasomotor response. In the inert group this did not occur or the response was paradoxical. The author explains this as the result of abnormal control by the higher nervous centres in the direction of stimulation (hyper-reactive group) or of inhibition (inert group).

Subtotal thyroidectomy resulted in a slow but progressive return to normal of the vasomotor responses. This required, in the hyper-reactive and some of the inert cases, 2 to 4 weeks; in the rest of the latter group, 3 to 4 months. Caffeine in doses of 0·2 g. before operation increased the responses in the inert group for about an hour, and after operation for much longer.

L. Firman-Edwards

1660. **Goitre among North African Immigrants in France.** (Le goitre des nord-africains transplantés en France)
P. GUINET and M. BERGER. *Lyon médical* [*Lyon méd.*] **188**, 253–265, March 29, 1953. 4 figs., 3 refs.

The authors have been struck by the high incidence of parenchymatous or juvenile goitre among North Africans working in the Lyons region of France. They have investigated a series of 27 such cases, brief clinical details of which are here presented, and have carried out tests with radioactive iodine in 4 of them.

The goitre was usually big enough to attract attention, the gland being diffusely enlarged. A thrill and bruit were frequently found, but were not indicative of hyperthyroidism—indeed no signs of hyperthyroidism were found in any of these patients. Fixation of orally ingested radioactive iodine in the thyroid was maximal in 8 hours, while its urinary elimination was slow, less than 12% being excreted in 48 hours in all 4 cases tested. Thyroidectomy was performed on 17 of the patients. Histological examination of the gland in these cases showed a predominantly hyperplastic appearance; colloid was absent, or present only in small amounts, and the epithelial cells were tall and their nuclei large. The remaining cases responded to treatment with thyroxine. No conclusions could be reached as to aetiology.

C. L. Cope

1661. **The Application of Radioactive Iodine in the Physiopathological Study of Goitre in the Young Patient.** (L'apport des techniques au radio-iode dans l'étude physiopathologique du goitre du jeune)
M. BERGER, P. GUINET, and R. MORET. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **29**, 1507–1520, May 6, 1953. 6 figs., 23 refs.

In this paper from the Lyons Faculty of Medicine the authors describe the investigation with radioactive iodine of 22 cases of clinically non-toxic goitre in patients ranging in age from 9 to 29 years. The cases examined fell into three groups. The first group consisted of 4 North Africans, recent immigrants into France [see Abstract 1660]. In these patients the goitre was of very rapid onset and was characterized by an increase in the uptake of radioactive iodine by the thyroid gland, with a thyrotoxic type of curve. The plasma protein-bound radioactive iodine content was also raised, and the urinary excretion of radioactive iodine was diminished. Thyroidectomy in 2 cases revealed a parenchymatous hyperplasia of the gland. In a third patient the goitre receded after 15 days' treatment with thyroxine. The authors consider that this type of goitre is due to central stimulation of the gland in response to an increased need for thyroid hormone, and that it is analogous to the thyroid hyperplasia of pituitary origin that can be produced experimentally by various means.

In the second group (13 patients), there was a high initial uptake of radioactive iodine by the gland, the curve of thyroid radioactivity rapidly reaching a plateau. The plasma protein-bound radioactive iodine level was low, and the urinary excretion of radioactive iodine diminished. The renal clearance of radioactive iodine was determined in 4 patients and was found to be subnormal. Histological examination of the thyroid in 2 cases revealed the picture of a colloid goitre. The authors postulate that in this type of case there is a high degree of retention and re-utilization of iodine, so that the thyroid store of iodine is increased. They suggest that the low level of plasma radioactivity may be due to a dilution effect.

The remaining 5 patients, constituting the third group, were not fully studied, but they differed from the others in that the urinary excretion of radioactive iodine was either normal or increased.

The authors discuss the relation between the types of goitre described and those due to iodine deficiency and to various antithyroid drugs. In particular, they describe the findings in 3 cases of hypothyroid goitre due to the administration of dimethyldithiohydantoin, an anticonvulsant drug. *G. Ansell*

1662. **The Use of ACTH and Cortisone in the Treatment and in the Differential Diagnosis of Malignant Exophthalmos: a Preliminary Report**
L. W. KINSELL, J. W. PARTRIDGE, and N. FOREMAN. *Annals of Internal Medicine* [*Ann. intern. Med.*] **38**, 913–917, May, 1953. 10 refs.

The results are reported in 9 cases of malignant exophthalmos associated with pituitary–thyroid disease treated with ACTH and cortisone over the past 2 years at the Highland Alameda County Hospital, Oakland, California. Although the case reports are lacking in detail [as might be expected in a preliminary report] the important features appear to be as follows.

1. All 9 patients improved within 48 hours of the beginning of treatment.

2. The dosage level of ACTH and cortisone was much higher than is usual for these substances. As would be expected, the incidence of complications from these large doses was high, and when local therapy was given this had to be very frequent—every one or two hours throughout the day.

3. ACTH and cortisone were without permanent effect on the unilateral exophthalmos of one patient, and it was subsequently found that he had a tumour of the orbit. *G. A. Smart*

PARATHYROID GLANDS

1663. **Tetany and Epilepsy.** (Tétanie et épilepsie)
H. GOTTA. *Presse médicale* [*Presse méd.*] **61**, 609–611, April 25, 1953. 4 figs., 7 refs.

In 15 out of 26 cases of tetany studied by the author the condition became chronic, and in 6 of these epileptic attacks occurred. In 4 of the 6 the tetany followed thyroidectomy and in the other 2 cases it was idiopathic in nature. In each case the onset of epilepsy followed that of tetany, the interval varying from 15 days to 5 years. The attacks in all 6 were typical of grand mal, but one patient also suffered from " vertiginous equivalents ". The electroencephalogram (EEG) was normal in 10 of the cases of tetany without epilepsy and in 3 of the 6 with epilepsy, but was considered to show epileptic features in the other 3. [One of these records is not convincing.] In each case the administration of calciferol suppressed both the tetany and the epilepsy, and in one case well-marked paroxysmal theta activity disappeared from the EEG.

The association of tetany and epilepsy is regarded by the author as more than fortuitous, hypocalcaemia acting as an epileptogenic factor. But as epilepsy is associated with tetany only in certain cases, other factors—probably constitutional in nature—must be involved. It is suggested that the possibility of latent idiopathic tetany should be considered, and that the serum calcium and inorganic phosphorus content should be determined, in every case of idiopathic epilepsy. If any evidence of tetany, latent or otherwise, is found, the administration of calciferol in doses of 5 to 10 mg. daily by mouth is recommended. *L. G. Kiloh*

1664. **Papilloedema and Fits in Hypoparathyroidism, with a Report of Three Cases**
D. K. GRANT. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **22**, 243–259, April, 1953. Bibliography.

The author describes in detail 3 cases in which symptoms of hypoparathyroidism developed after thyroidectomy for thyrotoxicosis in women aged 20, 33, and 38 years respectively at the time of operation. Their symptoms were inadequately controlled, and papill-

oedema developed after 5 years, 6 months, and 5 years respectively, for which they were admitted to the Royal Prince Alfred Hospital, Sydney. These 3 cases are compared with 28 similar cases which have been reported in the literature.

It appears that the papilloedema is almost invariably associated with increased cerebrospinal-fluid pressure, which is considered to be the result of cerebral oedema. It is also suggested that cerebral oedema is responsible for epileptiform convulsions and abnormal electroencephalographic recordings in hypoparathyroid tetany. Adequate treatment results in the disappearance of all symptoms. *A. C. Crooke*

ADRENAL GLANDS

1665. **Further Studies on Blood and Bone Marrow after Administration of ACTH and Cortisone.** [In English] N. G. Hävermark and N. G. Nordenson. *Acta haematologica* [*Acta haemat.* (*Basel*)] **9**, 227–237, April, 1953. 4 figs., 16 refs.

In 3 patients suffering from arthritis, for which treatment with ACTH and cortisone was given at the Södersjukhuset, Stockholm, changes in the blood and bone marrow were observed. There was stimulation of erythropoiesis and of the formation of polymorphonuclear leucocytes, but not of lymphocytes. Treatment with ACTH, and to a lesser degree with cortisone, produced eosinopenia. The observations were not quite constant, and this the authors consider was due to the fact that the 3 patients received different dosages of the hormones. They are unable to say if the finding that cortisone had a less profound effect than ACTH on the bone marrow and peripheral blood picture was due to an essential difference between the action of the two drugs, or whether it was because ACTH was given in a higher dosage. *H. Lehmann*

1666. **Haematological Changes in the Bone Marrow and Peripheral Circulation due to Treatment with Cortisone and ACTH.** (Modificazioni del quadro ematologico (midollare e periferico) in corso di cura con cortisone e ACTH)
R. Scalabrino, G. Curtarelli, and R. Bombelli. *Haematologica* [*Haematologica*] **36**, 823–875, 1952. 16 figs., bibliography.

At a Milan hospital careful serial examinations of the blood picture were made on a series of 32 patients with a variety of acute, subacute, and chronic rheumatic conditions, including a number with carditis, and certain other diseases, all of whom were treated with cortisone or ACTH for variable periods and with a variable dosage.

In 19 cases the total leucocyte count increased and in 11 it decreased. The lymphocyte count decreased in the majority of patients, although this decrease was not constant and did not always persist, and in the spleen and lymph nodes the lymphoid centres became less marked and less cellular when the hormones were given in large doses. The neutrophil granulocyte count increased in almost all cases, and that of eosinophil granulocytes decreased in most, but only temporarily. In the bone marrow the number of eosinophil cells showed no changes with treatment. A slight rise in the reticulocyte count occurred in 11 patients, and the haemoglobin level and erythrocyte count increased slightly—partly as a result of treatment, but possibly owing to a natural remission of the disease process in some cases.
E. Neumark

1667. **The Effect of Cortisone and ACTH on the Phagocytic Activities of Leucocytes and Macrophages.** (Untersuchungen über den Einfluss von Cortison und ACTH auf die Phagozytose der Leukozyten und Makrophagen)
S. Moeschlin, W. Zurukzoglu, and J. Crabbé. *Acta haematologica* [*Acta haemat.* (*Basel*)] **9**, 277–288, May, 1953. 3 refs.

At the University of Zürich the effect of ACTH (corticotrophin) and cortisone on the phagocytic activity of the leucocytes and the macrophages of rabbits was investigated.

Macrophages were obtained from a pleural exudate induced by the intrapleural injection of broth and gum arabic; the exudate was mixed with suspensions of *Staphylococcus aureus* and the number of cells containing ingested bacteria estimated after 30 minutes. ACTH or cortisone added *in vitro* had no effect on phagocytosis, but when either drug had been given to the animals for a week or more before the experiment there was slight but distinct inhibition, becoming more marked as the period of administration was increased. This result is attributed to a reduction in the production of macrophages and in the potency of chemotactic factors. In the blood of animals treated with cortisone, however, no inhibition of phagocytosis by the leucocytes could be demonstrated.
E. Neumark

1668. **Enhancement of Adrenocorticotrophic Activity**
H. Cohen, H. H. Freedman, W. Kleinberg, M. Eisler, and G. J. Martin. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol.* (*N.Y.*)] **82**, 749–751, April, 1953. 12 refs.

The authors present experimental evidence to show that the effect of a subcutaneous injection of ACTH (corticotrophin) on the adrenal cortex of the rat is enhanced by its administration in a medium which delays absorption of the hormone. Hypophysectomized Sprague–Dawley male rats of 110 to 115 g. body weight were used, each group being given a subcutaneous injection of 1 *U.S.P.* unit of ACTH dissolved in 0·5 ml. of one of the following test solutions: 0·2% suramin, 5% phosphorylated hesperidin, 2·5% phosphorylated hesperidin, 5% hesperidin methyl chalcone, 15% gelatin, 15% gelatin plus 20 T.U. of hyaluronidase, and 15% gelatin plus 4% phosphorylated hesperidin. Control animals received injections of the test solutions without ACTH. In each group the ascorbic acid content of the left adrenal gland was determined by the method of Mindlin and Butler 3 hours after the injection, and that of the right gland 6 hours after the injection, the effect of the ACTH being judged from the degree of depletion of adrenal ascorbic acid found.

Of the single agents tested, the most effective in enhancing the action of ACTH were phosphorylated hesperidin and heavy gelatin, while a combination of these two substances was even more effective, the maximum response being greater than with either agent alone and its appearance being delayed until the 6th hour. The possible mechanism of this delay of absorption was investigated *in vitro*, and the activity of phosphorylated hesperidin and hesperidin methyl chalcone in inhibiting the tryptic digestion of casein, as determined by the method of Anson (*J. gen. Physiol.*, 1938, **22**, 79), was shown to be similar in degree. It was therefore concluded that the delaying action of the former was due not to its antiproteolytic properties, but to its inhibiting effect on tissue hyaluronidase, the methyl chalcone of hesperidin having no such action. It is suggested, however, that the greater effectiveness of the combination of gelatin with phosphorylated hesperidin may be due to the antiproteolytic properties of the latter, the tissue proteinases being prevented from acting on the gelatin, which thus retains its depot effect for a longer period of time and reinforces the antihyaluronidase action of the phosphorylated hesperidin. *D. G. Adamson*

1669. **A Specific Water Diuresis Test for Adrenocortical Insufficiency**
S. Oleesky. *Lancet* [*Lancet*] **1**, 769–770, April 18, 1953. 1 fig., 17 refs.

Among laboratory aids to the diagnosis of adrenocortical insufficiency Kepler's test is considered the most useful, but it is complicated and tedious to perform. Soffer and Gabrilove (*Metabolism*, 1952, **1**, 504; *Abstracts of World Medicine*, 1953, **13**, 411) have proposed a simplified version of this test, but it is said to have the disadvantage that often the patient is unable to ingest the necessary quantity of water (1,500 ml.) without vomiting and that each of the two parts of the test lasts 5 hours. The present author now describes a modification of these tests which he claims is simpler to perform and more specific in its results.

Following overnight deprivation of fluid, the patient is asked to drink as much water as possible, up to a limit of 1 litre, in 20 minutes. The urine flow is then measured at intervals of 15 to 20 minutes for 2½ hours, the maximum rate of urine flow in adrenocortical insufficiency being less than 2 to 3 ml. per minute. The test is repeated next day 4 hours after the oral administration of 50 to 75 mg. of cortisone.

In performing this test it is necessary to observe the following precautions: (1) the patient's serum sodium level must not be very low, because then even the administration of cortisone will fail to produce a normal diuresis; (2) the dose of cortisone must not be less than 50 mg.; (3) the control and test observations must be made at the same time of day; and (4) the water should be drunk when the cortisone activity is at its highest level as measured by eosinophil depression (4 to 8 hours after ingestion in adrenal insufficiency).

The author gives reasons for regarding this test as better than other excretory tests and discusses its use in differential diagnosis. *Norval Taylor*

DIABETES MELLITUS

1670. **Lipodystrophy following Insulin Injections**
R. G. Paley. *Metabolism* [*Metabolism*] **2**, 201–210, May, 1953. 40 refs.

The author of this paper from the Department of Medicine, University of Leeds, describes two forms of lipodystrophy occurring in diabetics: (1) lipoatrophy, which consists in loss of subcutaneous fat at the site of injection of insulin and varies in extent from small areas of depression 2 to 4 cm. in diameter to large areas of fat loss; and (2) lipohypertrophy, with formation of a large subcutaneous mass of fat over which the skin is easily movable, and which often extends far beyond the site of insulin injection.

Lipoatrophy was found to occur in 102 (54·8%) of the 186 patients, the complication being of late onset—269±36·9 days from the first injection of insulin. The author found that lipoatrophy occurred more commonly with zinc protamine insulin, and that its incidence ran closely parallel with that of dermal reactions to insulin. It is suggested that dermal sensitivity may cease, but the "dermal reacting factor" may be retained in the subcutaneous tissues. Of the 102 patients, 30 showed some spontaneous improvement, and occasionally the regeneration was complete. The conflicting views on the aetiology of lipoatrophy are discussed.

Lipohypertrophy was observed in 12 (6·4%) of the 186 patients. The average age of these patients was 35 years, which is significantly younger than the mean age of the patients with lipoatrophy. Of the 12 patients, 5 showed pure hypertrophy, whereas in 7 there was a combination of atrophy and hypertrophy.

The author considers that lipoatrophy and lipohypertrophy are caused by similar mechanisms.

I. McLean-Baird

1671. **Comparative Effects of Insulin Administered Intravenously and Subcutaneously**
B. Beidleman, L. A. Principato, and G. G. Duncan. *Metabolism* [*Metabolism*] **2**, 211–217, May, 1953. 4 figs., 13 refs.

The authors have compared the effects of the subcutaneous and intravenous injection of insulin in 10 patients with well-stabilized diabetes mellitus and 10 hospital patients without diabetes and with no evidence of hepatic or endocrine disturbance. All the patients had nothing to eat or drink after 10 o'clock on the night preceding the test, and the fasting blood sugar level was determined before 7 o'clock the next morning. Soluble insulin in a dosage of 20 units was given subcutaneously at 7 a.m. on the first day of the test, and the patient then received 20 g. of carbohydrate by mouth every hour until 3 p.m. A normal diet was given after 3 p.m. and throughout the following day. On the third day the procedure was identical with that on the first day, except that 20 units of soluble insulin was given intravenously instead of subcutaneously. In the diabetic patients their usual amount of long-acting insulin was reduced to ensure a moderate hyperglycaemia at the start

of the test. In the non-diabetic patients intravenous injection of insulin caused an immediate fall in the blood sugar level averaging 34 mg. per 100 ml. by the end of 30 minutes, and a similar immediate fall was noted in the diabetic patients. A mild " overswing " hyperglycaemia above the fasting value was observed between the 3rd and 6th hours after intravenous administration of insulin in both diabetics and non-diabetics. When the insulin was given subcutaneously an entirely different pattern resulted, there being an average rise in the blood sugar level of 21 mg. per 100 ml. above the fasting value in both groups. It is considered that this is probably due to the effect of carbohydrate absorption before insulin given subcutaneously starts to act.

The authors conclude that their investigation supports the recommendation that in diabetic coma and circulatory collapse half the initial dose of insulin should be given intravenously. *I. McLean-Baird*

1672. **Glycolysis of Blood in Diabetic Acidosis**
D. M. KYDD, A. J. HEINSEN, P. M. HALD, and J. P. PETERS. *Journal of Applied Physiology* [*J. appl. Physiol.*] **5**, 647–657, May, 1953. 26 refs.

The authors, working at the New Haven Hospital, New Haven, Connecticut, have investigated the glycolytic activity of the blood in diabetic acidosis. It has been demonstrated that the concentrations of organic acid-soluble phosphorus (phosphate esters), sodium, and potassium in the erythrocytes are diminished in this condition. This is somewhat anomalous, as in most circumstances the degree of breakdown of the phosphate esters is inversely related to glycolytic activity, the latter being accelerated and the former retarded by the addition of inorganic phosphate or any alkali to the blood *in vitro*, while the reverse occurs on acidification. In the present investigation 50 ml. of venous blood was obtained from 17 patients with diabetic acidosis before treatment, and in some cases also during recovery. Of this, 25 ml. was defibrinated anaerobically by the method of Eisenman, and 15 ml. allowed to clot under mineral oil in a centrifuge tube and the serum subsequently withdrawn under mercury by Austin's technique. The serum was used for the estimation of carbon dioxide, inorganic phosphate, and other electrolytes, and the defibrinated blood for the determination of sugar, total acid-soluble phosphorus, and inorganic phosphate concentrations and cell volume. The remaining blood was divided into two 5-ml. samples; phosphate solution, insulin, or other agents were added to one, and both were incubated at 37·5° C. with constant agitation for an appropriate period, after which the above estimations were repeated. [For details of the methods used the original paper should be consulted.]

In 13 out of 24 samples the rate of glycolysis was normal (10 to 16 mg. per hour or greater), while in 3 none was demonstrated until after treatment. Addition of sodium or potassium phosphate caused an acceleration of the rate of glycolysis in all but 3 samples. Where glycolytic activity was low, the bicarbonate concentration of the serum was found to be low (2·8 to 5·1 mEq. per litre) and the blood sugar level high (782 to 1,380 mg. per 100 ml.), but equally abnormal bicarbonate and sugar levels were also found in cases in which glycolysis was normal. The concentration of phosphate esters was reduced in the cases where glycolysis was absent, and although no correlation was found, it was noted that a low rate of glycolysis was never associated with a normal or high blood phosphate-ester level. Where the addition of phosphate accelerated glycolysis it also retarded the breakdown of the phosphate esters, but the authors found that acceleration of this breakdown process occurred as the glucose content became exhausted, and it was retarded again as the phosphate esters were used up. The addition of crystalline zinc insulin had no effect except in a few samples of blood from patients with severe acidosis, in which its action was too inconsistent to be readily explicable. The fact that glucose is distributed equally between the cells and serum was demonstrated, and normal rates of glycolysis were found in cases of pituitary and adrenal hypofunction and of renal acidosis.

The authors conclude that the depletion of the organic acid-soluble phosphorus of the erythrocytes in diabetic acidosis is the result of impairment of glycolysis in the blood. *R. St. J. Buxton*

1673. **Interpretation of the Rapid Intravenous Glucose Tolerance Test in Normal Individuals and in Mild Diabetes Mellitus**
D. S. AMATUZIO, F. L. STUTZMAN, M. J. VANDERBILT, and S. NESBITT. *Journal of Clinical Investigation* [*J. clin. Invest.*] **32**, 428–435, May, 1953. 3 figs., 10 refs.

The results are reported of an investigation carried out at the Veterans Administration Hospital, Minneapolis, into the rate of disappearance of glucose from the blood of normal and diabetic subjects after a single intravenous injection, and into the value of the determination of this rate in distinguishing between the normal subject and the mild diabetic. A dose of 25 mg. of glucose (as a 30% solution in distilled water) was given intravenously within 4 minutes, the blood sugar level being estimated before the injection, 4 minutes after the injection, and then every 8 minutes for 72 minutes. The subjects consisted of 70 non-diabetic men aged 25 to 50 years with no family history of diabetes, 26 patients known to have mild diabetes, and 13 with severe diabetes.

In the normal subjects the rate of disappearance of the excess glucose was proportional to the amount by which its concentration exceeded the fasting level, and ranged from 3·00 to 4·84% per minute. By repeating the test after 3 months in 20 of these subjects and by repeating it with a larger dose of glucose (35 g.) in another 13 subjects it was shown that for each subject the rate of disappearance of glucose remained constant on repeated testing and was independent of the dose given. In the 26 mild diabetics, who were controlled by diet without insulin, the rate of disappearance was found to be significantly reduced, ranging from 0·93 to 2·46% per minute, while in the 13 severe diabetics the reduction was even more marked, the rates ranging from 0·23 to 1·64% per minute.

The advantages of this method of interpretation of the intravenous glucose tolerance test are discussed.

J. Lister

The Rheumatic Diseases

1674. **Natural History of Lupus Erythematosus Disseminatus**
R. A. JESSAR, R. W. LAMONT-HAVERS, and C. RAGAN. *Annals of Internal Medicine* [*Ann. intern. Med.*] **38**, 717–731, April, 1953. 1 fig., bibliography.

The introduction of cortisone and corticotrophin in the treatment of lupus erythematosus has emphasized the lack of real knowledge of the natural history of this disease. The authors have reviewed 44 cases of the disorder seen at the Columbia-Presbyterian Medical Center, New York, in the past 15 years, together with 279 reports published in the literature during the period 1948–52. The diagnosis of lupus erythematosus disseminatus in the authors' own cases was based on the 10 criteria laid down by Brenner *et al.* (*Amer. J. med.*, 1948, **5**, 288); and only those cases were selected from the literature in which at least 7 of these diagnostic criteria were fulfilled.

Information as to the presenting symptoms was available only in the authors' cases, arthralgia being observed in 48% of these, fever in 25%, malaise in 18%, loss of weight in 14%, skin lesions in 14%, and Raynaud's phenomenon in 11%. Fever was present at some time during the illness in nearly all the cases reviewed. Rashes were observed in 69% of the authors' cases and in 84% of those culled from the literature; arthritis or arthralgia in 76% and 77% respectively; and cardiac manifestations in 70% and 68% respectively. Comparative information relating to other symptoms and signs and to laboratory and necropsy findings is given. Of the authors' patients 13 (30%) were alive after 5 years. In the reports from the literature it was much more difficult to determine the time of onset of symptoms, but of cases in which assessment was possible, in 22% the patient was alive after 5 years. *R. E. Tunbridge*

1675. **The " Pararheumatic " Arthropathies**
H. H. FRIEDMAN, S. SCHWARTZ, M. TRUBEK, and O. STEINBROCKER. *Annals of Internal Medicine* [*Ann. intern. Med.*] **38**, 732–758, April, 1953. 8 figs., 35 refs.

The authors define the pararheumatic arthropathies as the musculo-articular manifestations occurring in the " pararheumatic " diseases—acute disseminated lupus erythematosus, polyarteritis nodosa, diffuse scleroderma, and dermatomyositis. After a full discussion of the relevant literature the authors review 36 cases of pararheumatic arthropathy admitted to the Bellevue Hospital, New York, from 1938 to 1947, describing 8 of them in detail. They stress the high incidence of arthropathy in the pararheumatic diseases and its frequency as a presenting symptom. In their opinion a pararheumatic disorder should be considered if a case of so-called fibrositis is associated with fever; also in acute or subacute polyarteritis of long duration accompanied by progressive deterioration, in fulminating polyarteritis, in atypical rheumatoid arthritis, and in all cases of arthritis associated with bizarre cutaneous manifestations.

[Although this paper serves to draw attention to the prevalence of arthropathy in the conditions named, the authors' attempts at classification do not advance our knowledge of these diseases or facilitate their diagnosis.]
R. E. Tunbridge

ACUTE RHEUMATISM

1676. **The Function of the Adrenal Cortex in Rheumatic Fever**
S. WIENER. *Australasian Annals of Medicine* [*Aust. Ann. Med.*] **2**, 103–106, May, 1953. 18 refs.

As a measure of adrenocortical function the author determined the eosinopenic response in a small series of children aged between 7 and 13 years admitted to the Children's Hospital, Melbourne, suffering from " the major manifestations of rheumatic fever, including chorea ". The response was estimated in 4 groups tested respectively with 10 mg. ACTH intramuscularly, 0·3 mg. adrenaline subcutaneously, and 60 and 30 mg. ephedrine sulphate given by mouth. Except for those receiving the smaller dose of ephedrine sulphate, all patients showed a significant fall in the eosinophil count after 4 hours. Control observations were made on the previous day, and the timing was arranged to avoid normal diurnal variations.

The author concludes that no evidence is given by this method of examination to suggest any hypofunction of the adrenal cortex or interference with the pituitary–adrenocortical relationship in rheumatic fever. The study was made with a view to substantiating " the presumed allergic reactions in rheumatic fever " based on the belief that ACTH and cortisone inhibit the delayed type of allergic reaction. As a secondary observation it was noted that the normal level of circulating eosinophil cells in this group was somewhat higher than the upper limit of normal defined by Discombe (*Lancet*, 1946, **1**, 195). *Harry Coke*

1677. **Sodium Salicylate in Rheumatic Fever; Effect of Adjuvant Medication**
L. L. HENDERSON. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **225**, 480–484, May, 1953. 20 refs.

Patients with rheumatic fever in a U.S. Army hospital and varying in age from 18 to 38 years were given 1·6 g. of enteric-coated sodium salicylate every 4 hours together with one of the following adjuvant drugs: sodium bicarbonate, magnesium trisilicate, aluminium hydroxide gel, and aluminium hydroxide tablets. Blood samples for salicylate determination were taken at 8 a.m. every second day.

In 24 cases receiving enteric-coated sodium salicylate alone an average plasma salicylate level of 42·2 mg. per 100 ml. (range 33·4 to 57·0 mg. per 100 ml.) was found. In a further 16 patients the administration of 1·6 g. of sodium bicarbonate together with salicylate depressed the plasma salicylate level, the average reading being 29·8 mg. per 100 ml. (range 24·9 to 37·0 mg.). Several of these patients complained of "bloating" and gaseous eructations. The average plasma salicylate level in 17 patients receiving 0·65 g. of sodium bicarbonate with each dose of salicylate was 35·9 mg. per 100 ml. (range 26·7 to 48·6 mg.); there were few complaints of gastric upset. In 13 patients receiving 1·0 g. of magnesium trisilicate with each dose of salicylate the levels ranged from 38·8 to 54·2 mg. per 100 ml., with an average of 43·0 mg; some of these patients with the higher concentrations suffered from dyspnoea, nervousness, and anorexia. The figures in 9 patients receiving aluminium hydroxide in tablet form were: average 46·5 mg. per 100 ml.; range 40·0 to 54·0 mg. In this group nervous irritability accompanying the higher salicylate levels was prominent. Of the 16 patients started on aluminium hydroxide gel, 8 to 16 ml. for each dose of salicylate, 5 became so nauseated that they could not continue. The average plasma salicylate level of the remaining 11 patients in this group was 49·8 mg. per 100 ml. (range 42·8 to 59·2 mg.).

Sodium bicarbonate was found to have the effect of restoring toward normal the diminished carbon dioxide combining power resulting from salicylate therapy. Magnesium trisilicate and aluminium hydroxide gel and tablets were as effective as sodium bicarbonate in relieving gastric distress, but did not lower the plasma salicylate level or raise the carbon dioxide combining power. Incidental observations were the apparent lack of effect of salicylate on the elevated erythrocyte sedimentation rate and the prolonged P–R interval, and the absence of any haemorrhagic manifestations.

Norval Taylor

1678. **Further Experience with Aureomycin in the Treatment of Acute Rheumatism in Children.** (Ďalšie skúsenosti s aureomycínovou liebčbou akútneho reumatizmu u detí)

L. Sikula. *Lékařské Listy* [*Lék. Listy*] **8**, 213–215, May, 1953.

The author reports his results in 35 children with acute rheumatism treated with aureomycin. Of these, 27 patients were observed for a period of 2 years, and are divided into three groups according to the progress made.

In the first group (4 children) 3 patients relapsed because treatment was too short, having lasted only 6, 5, and 10 days respectively, and the dosage was too low (0·5, 5, and 6 g. respectively). The fourth patient suffered a recrudescence of the acute rheumatic process, with decompensated mitral stenosis, 6 months after cessation of treatment, but became symptomless after a 12-day course of aureomycin (total dose, 8 g.).

In the second group (6 patients), treatment was begun in 3 cases 4, 28, and 14 days after the onset of the attack and lasted 16, 23, and 15 days, the dosage being 8, 16, and 16 g. respectively. In these 3 cases all clinical signs disappeared without any other antirheumatic treatment; the electrocardiogram, which had shown a myocardial change in the child in whom treatment had been started only after 28 days, returned to normal after 23 days. In the remaining 3 cases the erythrocyte sedimentation rate became normal after 11, 12, and 7 days of treatment with total doses of 12, 12, and 16 g. respectively. All 6 children were in good health 4 months after cessation of treatment.

In the 17 children in the third group no further attack occurred for 10 to 24 months, in spite of recurrent tonsillitis or infectious disease. Restriction of activities or school attendance was imposed on only 2 patients with compensated mitral stenosis; tonsillectomy was performed on 3 children. In 7 cases treated 4 to 14 days (average 8 days) after the onset of the first attack the cardiac findings were normal; in 4 patients treated 7 to 21 days (average 11 days) after the onset mild cardiac involvement was observed, while in 6 cases in which treatment with aureomycin was delayed up to 12 months after a repeated attack, severe mitral and aortic valvular disease was found. Nevertheless, in all cases the electrocardiogram was within normal limits at the time of follow-up examination.

The gain in weight amounted from 2·1 to 10 kg. (average 4·3 kg.), with a rapid weight increase of 7 to 10 kg. during prepuberty and puberty. Dental caries was found in 10 cases of the last group. The blood picture was normal in all children, and there was no complaint of joint or muscle pain. The author advises the continuation of treatment with aureomycin for a maximum of 28 days, with full dosage for 21 days. The effective dose seems to be 40 to 50 mg. per kg. body weight per day. Vitamin B or nicotinic acid was simultaneously given in all cases, and additional vitamin K in some of them. The degree of residual cardiac damage seemed to depend upon the time lag between the onset of the disease and the start of treatment. Nevertheless, even cases with severe cardiac involvement resistant to other antirheumatic therapy responded well. The treatment was well tolerated even by younger children. It is stressed, however, that aureomycin treatment cannot replace the therapeutic measures indicated in cases of disturbed circulation. In hyperactive cases with recurrent relapses repeated small transfusions of blood from women between the 4th and 6th months of pregnancy are advised.

M. Dynski-Klein

1679. **Antistreptolysin-O Serum Levels. Their Determination and Use as a Diagnostic Aid with Particular Reference to Active Rheumatic Fever in Children**

N. F. Hollinger. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **43**, 561–571, May, 1953. 1 fig., 32 refs.

Comparisons of the mean titre of antistreptolysin-O (AST) in the serum of non-rheumatic children and of children with active rheumatic fever have not hitherto revealed differences sufficiently great to provide a reliable diagnostic test, although a low or absent AST may provide confirmatory evidence of the absence of active

rheumatic fever. The present author, working at the University of California, attempted to discover whether a minimum titre could be established to provide a "diagnostic exclusion index". Serum was therefore obtained from individuals under 21 years of age, who were classified after examination (at a number of centres) as follows: 2,147 normal children, 2,988 with illness other than active rheumatic fever, and 197 with active rheumatic fever. AST determinations were made by the technique of Rantz and Randall, using stable, reduced, desiccated streptolysin-O, a number of different laboratories participating in the work. The reproducibility of results as between laboratories was tested and found satisfactory.

In all three groups there was a significant degree of variation in titre between sera from different parts of the United States. Nevertheless, analysis of the combined results for non-rheumatic subjects showed that in all but one of the geographical areas at least 30% of sera gave AST values of less than 100 units per ml., whereas less than 5% of sera from cases of active rheumatic fever gave AST values in this range. The author notes that of the AST values in 1,142 cases of rheumatic fever reported in the literature, all but 2 were above the level of 50 units per ml. He therefore suggests that a titre of 50 units or less per ml. obtained repeatedly in the same case is a highly reliable "exclusion index" for rheumatic fever.

[It is not clear from the text whether in selecting the cases of active rheumatic fever the duration of the disease was taken into consideration. If cases with activity of long duration were included, these results must be taken to support Coburn's original view that a rise in serum antistreptolysin titre is directly related to the activity of the disease.] *E. J. Holborow*

See also Bacteriology, Abstract 1503.

CHRONIC RHEUMATISM

1680. **An Investigation of Combined Treatment with ACTH and *para*-Aminobenzoic Acid in Rheumatoid Arthritis.** [In English]
O. Z. DALGAARD. *Acta endocrinologica* [*Acta endocr. (Kbh.)*] **13**, 39–54, May, 1953. 10 figs., 16 refs.

In view of various reports of the favourable effect of using *para*-aminobenzoic acid (PABA) as an adjuvant to cortisone in the treatment of rheumatoid arthritis, the author set out to determine whether a combination of PABA and ACTH (corticotrophin) had a similar synergistic or additive effect, and whether PABA alone influenced hormone production by the adrenal cortex. Accordingly 5 patients suffering from rheumatoid arthritis of long standing were treated at the Kommunehospitalet, Copenhagen, with PABA and small doses of ACTH. They were first given 10 mg. of ACTH and 12 g. of PABA daily for 5 days; then, after a 5-day interval, they received 10 mg. of ACTH daily for 5 days without PABA, and finally, after a further 5-day interval, the first course was repeated. The effect of treatment was assessed from clinical appearances and by determination of the eosinophil count and urinary 17-ketosteroid excretion.

The administration of these small doses of ACTH produced some slow symptomatic improvement in 4 of the 5 patients treated, with a rise in 17-ketosteroid excretion and a fall in eosinophil count, during the treatment periods, but the addition of PABA appeared to make no difference to the response.

A second group of 5 patients suffering from other diseases were given 12 g. of PABA daily for 5 days, the urinary 17-ketosteriod excretion being determined daily. The drug had no demonstrable effect. *G. Loewi*

1681. **The Treatment of Rheumatoid Arthritis with Hypoglycaemia.** (Hypoglykæmibehandling af polyarthroitis chron. prim.)
P. V. RIISING and J. E. HOLST. *Ugeskrift for Læger* [*Ugeskr. Læg.*] **115**, 558–561, April 9, 1953. 6 refs.

At Roskilde County and Municipal Hospital, Denmark, 15 cases of rheumatoid arthritis were treated by the induction of hypoglycaemia with insulin. Each morning for 4 weeks the fasting patient was given sufficient insulin to produce hypoglycaemic symptoms, a carbohydrate meal being given at the end of 3 hours unless the severity of the symptoms necessitated administration of glucose at an earlier stage. The status of patients was assessed on appearance and performance of joints and on the erythrocyte sedimentation rate before, during, and after the course of treatment. A great improvement was noted in 4 cases, slight improvement in 6, and no improvement in 5 immediately after the course. At a follow-up examination 4 to 9 months later, however, there was great improvement in one case, slight improvement in 4, and no improvement in 10.
B. Nordin

1682. **Splenectomy in Rheumatoid Arthritis**
C. LER. STEINBERG. *Annals of Internal Medicine* [*Ann. intern. Med.*] **38**, 787–813, April, 1953. 15 figs., bibliography.

It has been shown, both experimentally in animals and in the human subject, that hypophysectomy results in atrophy of the spleen and, conversely, that splenectomy leads to hypertrophy of the anterior pituitary gland. The author of this paper considers Felty's syndrome to be a variant of rheumatoid arthritis, and has observed a hyperplastic marrow associated with granulocytopenia or leucopenia in affected cases. He presents detailed reports of 3 cases of Felty's syndrome in which splenectomy was performed at the Rochester General Hospital, New York. In 2 of these there was marked improvement, not only in the blood picture but also in the arthritic condition, following operation. In the 3rd case similar improvement followed splenectomy, but leukaemia developed 3 years later. Short reports are also given on 3 further patients who developed Felty's syndrome but had been treated with cortisone or corticotrophin. In one case, although both the splenomegaly and the leucopenia disappeared during cortisone treatment, they returned 4 weeks after its cessation. In the remaining 2 cases splenomegaly developed after cortisone

and corticotrophin therapy respectively. In these cases treatment with the hormones led to a temporary improvement in the blood picture and a diminution in size of the spleen, but did not prevent the development of splenomegaly or result in permanent reversal of splenomegaly if already present.

Splenectomy appears to be the treatment of choice in cases of Felty's syndrome, and it is suggested that one effect of removal of the spleen may be to bring about hypertrophy of the anterior lobe of the pituitary and thus increase the natural supply of corticotrophin.

R. E. Tunbridge

1683. **Hydrocortisone and Inflammatory Rheumatism.** (Hydrocortisone et rhumatismes inflammatoires)
S. DE SÈZE, J. ROBIN, and N. DEBEYRE. *Revue du rhumatisme et des maladies ostéo-articulaires* [*Rev. Rhum.*] **20**, 298–302, April, 1953.

The authors report their results in a preliminary trial at the Hôpital Lariboisière, Paris, of hydrocortisone injected intra-articularly in 24 patients with rheumatoid arthritis, of whom 19 were already undergoing treatment with cortisone. Their observations suggest that the maintenance dose of cortisone may be considerably reduced if one or more joints in which active disease is persisting are treated locally with hydrocortisone. In 15 patients given intra-articular injections of hydrocortisone the pain, swelling, and stiffness diminished and sometimes disappeared, and in all of them it was possible to reduce the maintenance dose of cortisone without relapse. In one patient with ankylosing spondylitis accompanied by arthritis of a hip-joint, local treatment of the hip brought rapid relief, and it was found possible to reduce the maintenance dose of cortisone from 125 mg. to 75 mg.

Kenneth Stone

1684. **The Local Injection of Hydrocortisone in Articular and So-called Para-articular Rheumatism.** (L'hydrocortisone en injection *in situ* dans les arthroses et les affections dites para-articulaires rhumatismales)
S. DE SÈZE, J. ROBIN, and A. DENIS. *Revue du rhumatisme et des maladies ostéo-articulaires* [*Rev. Rhum.*] **20**, 303–308, April, 1953.

In this further series of 87 patients [see Abstract 1683] with rheumatic diseases treated at the Hôpital Lariboisière by intra-articular injections of hydrocortisone, the dose at each injection was 25 mg. and at first injections were given once weekly.

Of 25 patients with osteoarthritis of the knee the results were "very good" or "good" in 17 (68%). In 5 of these, 1, 2, or 3 injections brought amelioration lasting 1 to 2 months. In the 8 cases showing a less satisfactory response pain returned after each injection in from 1 to 3 weeks. In a group of 25 patients with osteoarthritis of the hip the results were less striking, but 14 cases (56%) were relieved. One patient obtained lasting relief after 5 injections; in others, relief after each injection lasted only 3 or 4 weeks. Hydrocortisone was also given to 21 patients with scapulo-humeral periarthritis. In cases with acute or subacute subacromial bursitis in which pain was the predominant feature, the effect was in every case excellent. It was less good in conditions of long duration in which there was much restriction of movement owing to adhesions.

Kenneth Stone

1685. **The Therapeutic Effect of Intra-articular Hydrocortisone Acetate. (A Report on 130 Cases of Inflammatory and Degenerative Rheumatism.)** (De l'effet thérapeutique de l'hydrocortisone-acétate intra-articulaire. (Rapport sur une thérapeutique de 130 cas de rhumatisme inflammatoire et dégénératif))
L. DE PAP and M. A. TEIXEIRA. *Revue du rhumatisme et des maladies ostéo-articulaires* [*Rev. Rhum.*] **20**, 285–297, April, 1953. 3 figs., 11 refs.

The effect of the intra-articular injection of cortisone is uncertain and transitory. Although hydrocortisone (Kendall's Compound F) has the same therapeutic properties as cortisone it is unexpectedly efficacious when applied locally. The authors report their results in 130 patients at the Instituta Reumatologia, Lisbon, suffering from a wide variety of rheumatic diseases, principally rheumatoid arthritis and osteoarthritis, and treated with hydrocortisone. The most effective dose for injection of large joints was found to be 25 mg., and for smaller joints 8 to 15 mg.

In cases of rheumatoid arthritis the inflammatory signs disappeared first; in some cases relief of pain, easier though restricted movement, and reduction in swelling lasted up to 3 weeks, but lessened after 7 to 10 days. In osteoarthritis the relief was more lasting. The return of symptoms is the deciding factor as to whether, and when, injections are to be repeated. In general they were given weekly in rheumatoid arthritis. The authors stress that the secret of success is that the injections shall be truly intra-articular, particularly in affections of the hip-joint; the technique is described in some detail. No generalized effects were noted, the action of the hormone appearing to be purely local: for instance, in no case of polyarthritis was improvement observed except in the joint treated.

The effect of hydrocortisone is not specific, as disorders of the most varied aetiology, such as traumatic conditions, osteoarthritis, rheumatoid arthritis, rheumatic fever, tenosynovitis, and sciatica respond equally well. In the 37 cases of rheumatoid arthritis all signs of activity of the disease disappeared in 6 patients after 6 to 8 injections, 29 patients were improved, and only 2 were unaffected. Improvement followed in all of 28 cases of osteoarthritis of the knee, and was good but less satisfactory in 17 cases of osteoarthritis of the hip. The authors point out that this therapy is not curative; relief of pain in an osteoarthritic knee, even for several months, does not imply cure, for the same morbid process continues; and in rheumatoid arthritis symptoms recur sooner or later when the injections of hydrocortisone are stopped.

Kenneth Stone

1686. **Histochemical Studies of Rheumatic Conditions. Observations on the Fine Structures of the Matrix of Normal Bone and Cartilage**
H. T. FAWNS and J. W. LANDELLS. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **12**, 105–113, June, 1953. 11 figs., 8 refs.

Traumatic Surgery and Orthopaedics

1687. **Pigmented Scars**
B. S. CRAWFORD. *British Medical Journal* [*Brit. med. J.*] 1, 969–971, May 2, 1953. 2 figs., 4 refs.

The author draws attention to the problem created by allowing pigmented material to be retained in a healing scar after injuries such as those sustained in road accidents or in industry as the result of minor explosions.

The pathology of the healing scar is described and the technique whereby pigment can be removed by immediate treatment is clearly given. It is obvious that this treatment is in many instances not applied, and failure in this respect will lead to the necessity for treating the established state, either by surface removal of the affected area or by actual excision. This excision may result in a defect requiring grafting, though in most cases it is capable of immediate closure. In either instance the procedure is time-consuming and can be rendered entirely unnecessary by adequate treatment of the initial injury. *Rainsford Mowlem*

1688. **Experimental Arterial Spasm in the Lower Extremities Produced by Traction**
W. T. MUSTARD and E. H. SIMMONS. *Journal of Bone and Joint Surgery* [*J. Bone Jt Surg.*] **35B**, 437–441, Aug., 1953. 7 figs., 5 refs.

1689. **Intra-arterial and Intravenous Blood Infusion in Hemorrhagic Shock. Comparison of Effects on Coronary Blood Flow and Arterial Pressure**
R. B. CASE, S. J. SARNOFF, P. E. WAITHE, and L. C. SARNOFF. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **152**, 208–212, May 16, 1953. 3 figs.

The effects on coronary flow of intra-arterial and intravenous transfusion were compared in experiments carried out at Harvard School of Public Health on dogs in which the left main coronary artery was connected through a flow-meter to the right femoral artery. The animals were bled into warmed reservoirs from the left femoral vein until the required degree of hypotension and depression of coronary flow was obtained, and the blood then returned into either the femoral artery or the femoral vein. The pressure in the auricles, pulmonary artery, and the left femoral artery was recorded electromanometrically.

When 4 successive periods of hypotension and decreased coronary flow were treated alternately by return of the blood into the arterial and venous systems, it was noted that the speed and extent of recovery of coronary flow and arterial pressure were much the same whichever route was used and whether the period of hypotension was brief or long. In one case a rapid intra-arterial infusion failed to achieve an improvement in the condition of a dog which had been bled to a state of extreme haemorrhagic shock, and only direct coronary infusion brought about recovery.

The authors, while acknowledging the difference between purely experimental and clinical conditions, conclude that it is only the rapidity with which intra-arterial transfusion is carried out that gives it any superiority over the intravenous route. They suggest that except when there is mechanical obstruction in the heart (as during mitral valvotomy) or when cardiac arrest is almost complete there is no reason why the former should be more effective in improving the coronary circulation; nor do they see any reason why blood should not be given with equal rapidity intravenously as intra-arterially, thus avoiding the hazards of arterial spasm and necrosis. *J. S. Campbell*

1690. **Clinical Use of a Complex Method of Restoring Vital Functions in Severe Shock, Terminal States, or Clinical Death.** (Применение в клинике комплексной методики восстановления жизненных функций организма, находящегося в состоянии тяжелого шока, агонии или клинической смерти)
V. A. NEGOVSKII. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **31**, 3–11, April, 1953. 3 figs.

Russian medical science has for many years been concerned with the pathology and treatment of terminal states. This article gives details of the present methods employed and their indications. The most important contribution has been the introduction of the use of retrograde intra-arterial injection of blood under pressure. As early as 1876, Kievsky undertook a series of intra-arterial transfusions of defibrinated blood in severely wounded soldiers; in 1913, Andreev evolved an experimental method of centripetal intra-arterial injection of nutritive solutions with the aim of restoring the vital functions of the organism. From these beginnings has been developed the modern method of injecting conserved blood by the same route. To 250 ml. of blood is added 50 ml. of 40% glucose and 0·5 ml. of 3% hydrogen peroxide. Some 15 to 20 seconds after the beginning of the injection 0·5 to 1·0 ml. of 0·1% adrenaline is introduced through the rubber tubing of the apparatus. Injection is started at a pressure of 60 to 80 mm. Hg which is raised after 8 to 10 seconds to 180 to 220 mm. Hg, the pressure being regulated by a rubber bulb and recorded by a manometer connected by a T-tube with the blood container. The injection is made through a needle inserted into the brachial, radial, posterior tibial, or other artery, and the amount injected depends upon the nature of each individual case; for example, in a case of sudden collapse during operation with fall of blood pressure, 100 to 200 ml. would probably suffice.

In many cases, in addition to the intra-arterial injection of blood, artificial respiration may be necessary. The ideal way of performing this is with an intratracheal tube, using an anaesthetic apparatus in which oxygen is substituted for anaesthetic; failing this, manual artificial respiration is preferable to giving oxygen through

a mask, since it is difficult to control the tongue with the latter method. A pneumatic jacket of the Bragg–Paul type is also mentioned. [The Drinker type of respirator is not mentioned, perhaps because it would make difficult the employment of simultaneous blood injections.] Stimulation of respiration by pharmacological means or by "carbogen" (3·5% carbon dioxide and 96·5% oxygen) is contraindicated, as the bulbar reflex centres are unable to respond to such stimulation. In terminal states due to severe haemorrhage, intravenous blood transfusion should be given in place of intra-arterial injection as soon as the cardiac action has been sufficiently restored.

For some days after restoration it is necessary to watch the blood pressure, and if this falls, intra-arterial injection should be repeated as required. The indications for this method of treatment are: (1) agonal states or apparent death as a result of massive haemorrhage; (2) severe shock; (3) severe trauma; (4) severe toxaemia; (5) asphyxia; or (6) accidental electrocution. Contra-indications are severe head injuries, and other injuries incompatible with life. The author states that the literature up to date records recovery of 46·5% of 1,714 persons treated by intra-arterial injection for various terminal states, the recovery rates for specified conditions being 57% for severe shock (1,190 cases), 45% for agonal states (227 cases), and 18·1% for apparent death (116 cases). In the last-named condition the author emphasizes that treatment must be started not later than 5 or 6 minutes after the occurrence of apparent death. In the period following restoration of vital functions it is important to avoid any but the lightest of narcosis, overheating of the patient, and the tight bandaging of the limbs, which last may lead to gangrene.

L. Firman-Edwards

1691. **The Nature of Circulatory Failure in Accidental Death**

H. G. Swann, R. Anigstein, and C. C. Clark. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **225**, 475–479, May, 1953. 1 fig., 17 refs.

Acute circulatory failure has been attributed by some authorities to a peripheral vasomotor collapse secondary to severe anoxia and acidosis, while others believe that it is caused by primary myocardial failure. To obtain further evidence the authors, working at the University of Texas Medical School, examined dogs made anoxic by breathing pure nitrogen. Resuscitation was carried out when the blood pressure had fallen to between 80 and 90 mm. Hg, a point found from previous experiments to be critical for eventual recovery. The circulation was then arrested by the electrical production of ventricular fibrillation and, after clamping the aortic root, blood for analysis was immediately taken from the left ventricle and the ascending and abdominal aorta.

Blood from the left ventricle had an oxygen saturation of 82%, that from the ascending aorta 59%, and that from the abdominal aorta only 12% (average of 6 experiments). Thus reoxygenated blood had reached the left heart and ascending aorta, but had not reached the abdominal aorta in any quantity. It is argued that circulatory recovery entails reoxygenation of a myocardium failing from anoxia rather than the reoxygenation of the peripheral vascular tree presumed to have undergone vasomotor collapse, since recovery was already occurring before peripheral oxygenation had developed.

Keith Ball

1692. **Bilateral Protrusio Acetabuli. A Progressive Deformity from Infancy**

J. F. Brailsford. *Journal of the International College of Surgeons* [*J. int. Coll. Surg.*] **19**, 555–567, May, 1953. 10 figs., 5 refs.

The author contends that protrusio acetabuli is a progressive deformity, often beginning in childhood. In its early stages it may easily escape recognition, for the symptoms and signs in childhood resemble those of the more common hip disorders. Diagnosis depends on certain characteristic radiological findings. The "ilio-femoral line", described by the author, is broken, and the tear-drop outline of Kohler is compressed or absent; Shenton's line is not disturbed; in adult life secondary osteoarthritic changes are usually present. [For detailed information about the radiological changes the original article should be consulted.] Protrusio acetabuli may occur in association with Perthes's disease and slipping of the upper femoral epiphysis, and it may follow tuberculosis of the hip-joint, osteomalacia, Paget's disease, suppurative arthritis, and other abnormalities of the hip and pelvis.

The condition is well illustrated in the accompanying radiographs. *J. S. Batchelor*

1693. **Raw Egg Yolk as a Supplement to *X*-ray Therapy in Osteogenic Sarcoma in Children (under 18 Years Old) between May, 1950, and May, 1952.** (Rå aeggeblommer som supplement til røntgen-behandling af osteogene sarcomer hos børn (patienter under 18 år) fra 1/5 1950–1/5 1952)

C. Krebs. *Ugeskrift for Læger* [*Ugeskr. Læg.*] **115**, 1107–1132, July 16, 1953. 57 figs.

1694. **Cortisone as an Adjunct to Surgery in the Treatment of Keloids**

P. Clarkson. *Lancet* [*Lancet*] **1**, 923–926, May 9, 1953. 7 figs., 6 refs.

In experimental incised wounds cortisone and ACTH have been shown to suppress all the exudative and cellular reactions of healing. On the ground that a keloid is basically an extravagant deposit of intercellular fibres, the author gave cortisone to 8 patients with this condition. Following surgical excision, 5 cases were treated with cortisone given systemically, 100 mg. daily from the 5th to the 20th day. In the other 3 cases 25 mg. of cortisone acetate was applied locally daily over the same postoperative period. One really good result was balanced by one frankly poor one, but the scars in the remaining 6 cases gave a general impression of being softer and paler than previously.

The results in this series are admittedly inconclusive, but the effects of higher, and possibly near-toxic, dosage are still to be investigated. *R. P. G. Sandon*

Neurology and Neurosurgery

1695. **The Electromyographic Diagnosis of Myasthenia.** (Diagnostic électromyographique de la myasthénie)
F. THIÉBAUT, F. ISCH, and C. ISCH-TREUSSARD. *Revue neurologique* [*Rev. neurol.* (*Paris*)] **88**, 3–17, 1953. 4 figs., 12 refs.

At the Institute of Physiology, Strasbourg, 10 cases of suspected myasthenia gravis were studied electromyographically. The muscular action-potentials were recorded with a Bronk coaxial needle electrode in the extensor digitorum communis muscle in all cases, and in addition in the flexor communis in 2 cases and in the masseter in another 2 cases. After the records of 10 contractions against resistance had been obtained an injection of 0·5 mg. of " prostigmin " (neostigmine) was given; if the patient was already under treatment with neostigmine this was discontinued on the previous evening. Amplification was in 4 stages on to a cathode-ray oscillograph, the tracing being recorded in a camera on sensitive paper traversing at a speed of 12 or 25 cm. per second.

The typical myasthenic electromyogram consists of an initial burst of fine waves whose amplitude rapidly diminishes, sometimes ceasing rapidly, sometimes being prolonged by an intermediate type of tracing of variable duration with different groupings of motor units discharging. In many cases the initial record is not diagnostic. The response to neostigmine, however, is almost always more definite, as the drug causes an increase in the number of motor units that are active, a prolongation of the time for which a contraction is maintained, and delay in the onset of fatigue. In the cases studied these changes, which are peculiar to myasthenia gravis, were seen in all cases, although in some the record before neostigmine was given could not be distinguished from a normal electromyogram. In only one case out of 10 was a suspected diagnosis of myasthenia not confirmed, and this was in a woman whose only initial symptom had been diplopia. *Donald McDonald*

1696. **Cerebral Vascular Insufficiency. An Explanation of Some Types of Localized Cerebral Encephalopathy**
E. CORDAY, S. F. ROTHENBERG, and T. J. PUTNAM. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] **69**, 551–570, May, 1953. 5 figs., bibliography.

It is the purpose of this paper to establish a new entity only vaguely recognized by authors in the past, namely, cerebral vascular insufficiency. This transient condition has been demonstrated by experiment. Electroencephalograms were taken after the carotid vessels were partially or completely ligated in the monkey. When the blood pressure was lowered by bleeding the animal, focal electroencephalographic changes occurred on the side of the ligation, similar to those found in hemiplegia. When the blood pressure was restored, the electroencephalographic records returned to normal. These changes were proved to be due to a drop in blood pressure, rather than purely to anemia.

Clinically, cerebral vascular insufficiency occurs in hemorrhagic shock, coronary shock, surgical and traumatic shock, hypotension due to sympathetic block, and Smithwick sympathectomy, postural hypotension, carotid sinus stimulation, spinal anesthesia, and cardiac surgery. It also can occur as a result of miscellaneous extracranial factors, such as surgical ligation of the carotid arteries, spontaneous thrombosis of the internal carotid artery (Denny-Brown syndrome), gravitational states, as in flying, and the use of antihypertensive drugs. The changes which occur are transient if the blood pressure is restored to normal within a short period. The electroencephalographic changes and symptoms of cerebral origin, such as hemiplegia and hemianesthesia, will then usually disappear. If the blood pressure is not promptly restored to normal in patients with cerebral arteriosclerosis or congenital anomalies, focal changes will be permanent. As in the heart in which coronary arteriosclerosis has occurred, it is important to maintain the cerebral blood pressure at normal levels, especially in the elderly patient with narrowing of cerebral arteries. —[Authors' summary.]

1697. **A Study of Epilepsy due to Cerebral Tumour.** (Étude sur l'épilepsie des tumeurs cérébrales)
J. E. PAILLAS, J. BONNAL, and J. CORRIOL. *Revue neurologique* [*Rev. neurol.* (*Paris*)] **88**, 18–29, 1953. 12 refs.

In this series of 170 cases (111 in men and 59 in women) of epilepsy caused by cerebral tumour, reported from the Neurosurgical Clinic, Marseilles, 100 of the patients were in the age groups between 30 and 50, while only 15 were aged less than 20. The cases formed part of a series of 405 cases of cerebral tumour, giving an incidence of epilepsy of 41·9%. Sites most frequently involved were: temporal lobe 62, frontal lobe 40, and parietal lobe 50; virtually all the tumours were supratentorial. Histologically, the type of tumour most commonly the cause of the epilepsy was a benign tumour, the largest groups of these consisting of 57 cases of benign astrocytoma and 34 of meningioma, while malignant glioma was the cause in 33 cases. The most frequent types of attack were uncinate (temporal) fits in 70 cases, grand mal fits in 66 cases, and focal motor (Jacksonian) attacks in 60 cases. The electroencephalograms showed typical epileptic activity in only 25% of the cases with malignant tumour and in 38% of those with benign tumour. Of the 170 patients, 49 died as the result of operation, a mortality of 28·8%; in 21 of 48 cases followed up (43%) the epileptic manifestations persisted after operation.
Donald McDonald

1698. **Subdural Fluid Complicating Bacterial Meningitis** R. J. McKay, F. D. Ingraham, and D. D. Matson. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **152**, 387–391, May 30, 1953. 5 figs., 11 refs.

The authors believe that the accumulation of subdural fluid of high protein content with subsequent membrane formation which frequently occurs in the course of bacterial meningitis is responsible for many of the chronic neurological and psychiatric complications of this condition. At the Children's Medical Center (Harvard Medical School), Boston, 50 children with subdural fluid complicating bacterial meningitis were studied. The presence of subdural fluid was suspected and burr holes were made if the culture of the cerebrospinal fluid remained positive after 48 hours or if pyrexia persisted for 72 hours after the beginning of adequate treatment, if there were focal convulsions at any time, if fits or vomiting occurred in convalescence, if there was any gross neurological abnormality, or lastly if the course of the illness appeared unsatisfactory. An accumulation of subdural fluid was found in 30 (60%) of the patients, who were under the age of one year.

The fluid was usually xanthochromic with a high protein content, and in 8 cases it was infected with the causal organism. It was aspirated repeatedly, but in 42 of the 50 cases craniotomy was necessary to remove subdural membrane. In most cases this was followed by remission of the symptoms. Operation was delayed until the meningitis was well controlled, and anticonvulsants were given for at least 2 weeks subsequently.

L. G. Kiloh

1699. **The Treatment of Trigeminal Neuralgia by Negative Induction.** (О лечебном действии отрицательной индукции при невралгиях троиничного нерва) V. S. Khrapov. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **53**, 301–305, April, 1953. 4 figs., 5 refs.

The author has had some success in the treatment of trigeminal neuralgia by applying to the area of skin bordering on the sensitive points a low-frequency electrical discharge produced by means of a simple, specially designed apparatus, details of which are given.

L. Crome

1700. **Treatment of Pelvic Disturbances due to Lesions of the Spinal Cord and Cauda Equina by Ionization with Pilocarpine and Atropine.** (Лечение тазовых расстройств при поражении спинного мозга и конского хвоста ионогальванизацией с пилокарпином и атропином) V. A. Smirnov. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **31**, 63–67, Jan., 1953.

Injuries and disease involving the spinal cord and cauda equina are often associated with pelvic disturbances, including rectal and vesical incontinence, retention and urgency of micturition, failure of erection and ejaculation, and spermatorrhoea. The author treats such cases by ionization with pilocarpine or atropine, according to the indications, and claims some success in a series of 55 patients—41 men and 14 women—of whom 28 were suffering from gunshot wounds and 4 from other injuries of the spine, 7 from compression of the cord by tuberculous spondylitis, 5 from myelitis (non-specific), 5 from tabes dorsalis and cerebrospinal syphilis, 4 from disseminated sclerosis, and 2 from tumours of the spinal cord. Various levels of the cord were involved; in 20 cases the lesion was above the lumbar spine, in 6 in the lumbar vertebrae or caudal roots, in 13 in the lumbosacral region with involvement of the cauda equina, in 9 in the cauda alone, and in 7 undefined. Lesions of the higher levels were of the upper neurone type, those of the cauda of the lower-neurone type, while those of the lumbo-sacral region were of a mixed type. Three-quarters of the patients had urinary infections.

The positive electrode was placed over the lumbosacral spine, as low as possible, and the negative electrode over the symphysis pubis. A 0·1% solution of atropine sulphate (in cases of incontinence) or a 1% solution of pilocarpine chloride (in those of retention) was poured on to a pad, which was applied to the anode. A current of 0·2 or 0·3 mA per sq. cm. of electrode was passed for 35 to 40 minutes, and the treatment repeated the next day with the electrodes reversed. Improvement usually started after 5 or 6 treatments, a total of 10 to 16 being given. Atropine ionization was accompanied by dryness of the skin and mucous membranes, and that of pilocarpine by salivation.

Of the 55 patients, 15 were completely relieved of their pelvic symptoms and 24 much improved; 9 obtained temporary relief only and 7 were unrelieved, 6 of these 16 being cases of gunshot wounds, 4 of tuberculous spondylitis, 2 of myelitis, 2 of disseminated sclerosis, and 2 of spinal tumour. Four cases are described, one of retention and 3 of incontinence, in which restoration of normal function is reported, lasting 3 months to 2 years after cessation of treatment. The author explains the effect as being due to the local action of the drugs on the visceral ganglia.

L. Firman-Edwards

1701. **The Clinical Picture of the Vertebral Nerve Syndrome.** (К клинике поражений позвоночного нерва) O. V. Egorova. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **53**, 295–300, April, 1953.

Five cases of the vertebral nerve syndrome are described in which the main symptoms were occipital pain and tenderness, vertigo, tinnitus, early onset of mental fatigue, absent-mindedness, and insomnia; some of the patients also complained of clicking noises in the head and of nausea. The course of the syndrome was continuous and was punctuated by occasional vascular crises in the form of hypotension and flattening of the blood sugar curve. The author suggests that the syndrome, which was first described by Barré, is caused by neuritis of the vertebral nerve, which forms a part of the plexus surrounding the vertebral artery. One of the patients gave a history (and also had some evident signs) of lead poisoning, and another of cholecystitis. Treatment by prolonged sleep, or by *x* irradiation applied to the region of the vertebral artery, was effective.

L. Crome

Psychiatry

1702. **Pain in the Trunk**
J. CYRIAX and J. GOULD. *British Medical Journal* [*Brit. med. J.*] **1**, 1077–1081, May 16, 1953. 2 refs.

Patients with purely psychiatric disorders may be given physiotherapy for some years before the true nature of the disorder is recognized; in the same way symptoms of organic origin in a neurotic patient may be wrongly dismissed as psychiatric. Considerable difficulty in diagnosis often arises when the complaint is of pain in the trunk.

In this paper a scheme for the physical examination of such patients, with 11 diagnostic steps, is presented. According to the authors, a psychogenic illness may manifest itself in the patient's response to these procedures. Some types of back pain of emotional origin are described, such as the complaint of pain " all over ". Criteria for differentiation of " physical " pain from " psychogenic " pain are suggested, these being derived from a consideration of description, localization, precipitants, relieving factors, and previous history. The authors consider that the diagnosis of organic pain in a patient with psychiatric illness should be simple enough. In their experience the coexistence of causal and emotional factors in the aetiology of trunk pain is uncommon. Six illustrative case records are given.

[This is a practical, sensible, and useful article. The section on examination should be read by all those interested in stress disorders of the locomotor system.]

Desmond O'Neill

1703. **Transvestism. Hormonal, Psychiatric, and Surgical Treatment**
C. HAMBURGER, G. K. STÜRUP, and E. DAHLIVERSEN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **152**, 391–396, May 30, 1953. 9 refs.

True transvestists or eonists—persons with an irresistible desire to dress in the clothes of the opposite sex—are distinct from fetichists and passive homosexuals. The transvestist possesses " all the attributes of a feminine personality in a masculine body ". The condition is rare, but affects all races, and persons in all levels of society. The authors, writing from the University of Copenhagen, describe in detail the case of a man of 24 years who became depressed and contemplated suicide as a result of his difficulties. Typically, he refused to take testosterone for he did not want to be " cured " but merely to be enabled to live as a woman. The patient became " free from mental stress and psychically at ease " when given oestrogenic substances. After 2 years, castration was performed, and subsequently his penis was amputated and the scrotum transformed into a vulva-like structure.

The authors believe that as nothing can be done to alter the basic condition, it is justifiable to make life as tolerable as possible. In Denmark and Sweden permission has on rare occasions been granted to such patients to wear women's clothing and to live and be registered as women. Other measures worth considering are the administration of oestrogenic substances, castration, demasculinization, and the formation of an artificial vagina.

L. G. Kiloh

1704. **An Evaluation of the Use of Tetraethylthiuram Disulfide in the Treatment of 560 Cases of Alcohol Addiction**
E. C. HOFF and C. E. MCKEOWN. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **109**, 670–673, March, 1953. 1 fig.

At the Medical College of Virginia Hospital, Richmond, 560 patients were treated for alcoholism with tetraethylthiuram disulphide (disulfiram), the results being compared with those in a control group of 230 patients who were treated during the same period by other methods. Each patient in the first group took disulfiram for 4 days and was then given a test dose of whisky while under close observation. The authors emphasize that this test dose was given once only, to show the patient the effect of alcohol while under treatment, and did not create an aversion to alcohol. After the test the patient was maintained for about a year on a daily dose of 0·25 g. of disulfiram, with sedatives if necessary, and received psychotherapy as an out-patient.

After a period of follow-up varying from a few months to 2½ years, it was found that 78% of the patients treated with disulfiram had benefited, compared with 48% of the controls. It was also found that the prognosis was best for patients in the age group 40 to 45 years, and was better for men than for women. The authors conclude that " as an adjunct to a comprehensive plan of therapy . . . [disulfiram] is of value in selected patients amenable to voluntary treatment ".

J. Harper

1705. **Myanesin in Psychiatry**
A. B. MONRO and H. H. STEADMAN. *Journal of Mental Science* [*J. ment. Sci.*] **99**, 285–287, April, 1953. 4 refs.

The effect of administration of mephenesin (" myanesin ") in psychiatric disorders was investigated at Long Grove Hospital, Epsom. The drug was given in the form of an elixir to 68 patients suffering from anxiety symptoms, the dosage aimed at being 1 g. three times a day, although it was found advisable to start with 0·5 g. or less twice daily. The average duration of treatment was 6 to 8 weeks. In 28 patients the clinical results were good. The authors are careful to point out, however, that the previous personality of the majority of these 28 had been assessed as " excellent " or " good " and that the duration of the illness was generally less than a year.

The authors consider that mephenesin is a useful adjuvant to psychotherapy and other remedial measures in the treatment of anxiety states.

F. K. Taylor

Dermatology

1706. **Vitamin D_2 in Treatment of Nontuberculous Chronic Skin Diseases**
E. A. STRAKOSCH. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph. (Chicago)*] **67**, 496–502, May, 1953. 33 refs.

At the Presbyterian Hospital, Denver, Colorado, 108 patients ranging in age from 2 to 56 years and suffering from various types of non-tuberculous skin diseases were treated by massive doses of vitamin D_2 (calciferol) with the following results. In 57 patients with atopic dermatitis the results were encouraging, 42 being considerably improved, although none was completely cured. A small number of these, who had responded initially to the vitamin and relapsed after cessation of therapy, were again benefited by a second course, whereas a control group receiving a placebo were largely uninfluenced. The treatment with calciferol should be abandoned if there is no response within 3 or 4 months.

The results in the treatment of psoriasis (31 cases) were thought to be sufficiently encouraging to warrant a trial on a larger group of patients. Similar conclusions were arrived at for acne conglobata (3 cases) and lichen planus (11 cases). Patients with granuloma annulare and keloid did not appear to benefit by the treatment. Untoward reactions were observed in only 5 of the 108 patients. Withdrawal of the drug was sufficient to control these reactions and it was possible to restart the course at a lower level of dosage without further difficulties. *G. W. Csonka*

DERMATOSES

1707. **Observations on Six Cases of Dermatomyositis.** (Remarques à propos de six cas de dermatomyosite)
P. DE GRACIANSKY. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **29**, 1621–1633, May 20, 1953. 9 figs.

The author describes in detail, with very full case histories, 6 personal cases of dermatomyositis treated at the Hôpital Broca, Paris. The site, extent, and appearance of the skin lesions and the extent of the muscular involvement (consisting of asthenia, wasting, and painful semi-contractures) varied from case to case as did the duration of the illness, the latter ranging from 3 to 17 years. In some cases the muscle wasting was obscured by overlying oedema. Additional features observed were: marked colonic distension, indicating involvement of the visceral muscle, in 2 cases; osteoporosis in 2 other cases, in one of which there was also calcification of all the soft layers of the chest wall; and in one case root pains with paralysis of the soft palate and other neurological signs. The response to treatment varied considerably. One patient has remained well for 5 years after a single course of injections of iodized oil, while another has required repeated courses of the same compound; one patient died after transitory improvement in response to adrenaline and "syncortil". Treatment with ACTH and cortisone was successful in one severe case, but only partly so in another.

The author then considers at length the nosological problem, the absence of a common aetiology, and the differences between the skin lesions of subacute dermatomyositis of the type described by Wagner and by Unverricht and of poikilodermatomyositis of Petges. Since an erythemato-oedematous plaque often precedes poikilodermia, and acute dermatomyositis is often followed by a short and transitory poikilodermia, the two conditions are probably distinct although they have admittedly many points in common. The different clinical course also justifies the nosological differentiation, which, however, as the author points out, in the absence of a known aetiology is purely speculative. In contrast to the cases described, in which skin, muscle, and even bone and nerve were involved, there occur also monosymptomatic cases in which the skin or muscles alone are affected. Histologically, the muscle lesions consist of Zenker-type degeneration and lymphocytic infiltration; the skin lesions, which are more complex and are discussed in detail, are quite distinct from those of scleroderma, but share certain features with disseminated lupus erythematosus.

Laboratory investigations carried out in the author's cases showed that the fasting blood lactic acid level was raised at rest and increased less after exercise than in normal control subjects. The blood pyruvic acid level was normal, but 17-keto- and 17-oxysteroid excretion was low. Whereas in lupus erythematosus and in other collagen diseases there is usually a decrease in serum albumin level with an increase in gamma globulin, electrophoretic studies in 4 of the present cases showed a decreased serum albumin content without increase of gamma globulin. *Ferdinand Hillman*

1708. **The Treatment of Dermatitis Herpetiformis with Diaminodiphenylsulphone (DDS).** (Behandeling van dermatitis herpetiformis met diaminodiphenylsulfon (D.D.S.))
E. E. KRUIZINGA and H. HAMMINGA. *Nederlandsch tijdschrift voor geneeskunde* [*Ned. T. Geneesk.*] **97**, 1064–1068, April 25, 1953. 16 refs.

The treatment of 12 cases of dermatitis herpetiformis with 4 : 4-diaminodiphenylsulphone (DDS) at the Dermatological Clinic of the University of Groningen is reported. All but one of the patients in this series could be maintained free from symptoms with DDS, the requisite dose for adults being generally 50 mg. twice daily. Cessation of treatment resulted in a prompt recurrence of symptoms, which could again be rapidly suppressed by its resumption. No toxic phenomena of moment were encountered. While the series was too

small and the period of observation (average 5 months) too short for proper evaluation of the results, the authors consider that further experience will show the results of DDS therapy to surpass those obtained with sulphapyridine. Experience of the drug's use in leprosy would seem to indicate its suitability for prolonged treatment.

R. Crawford

1709. **Follicular Lichen Planus (Lichen Planopilaris)**
H. SILVER, L. CHARGIN, and P. M. SACHS. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph. (Chicago)*] **67**, 346–354, April, 1953. 4 figs., 11 refs.

In this paper, in which the authors attempt to clarify the syndrome known as follicular lichen planus, they describe 4 cases and analyse 101 cases culled from the literature. After a historical review of the syndrome under its various names, the clinical picture of the disease, the histopathological aspects, and the features that have given rise to controversy throughout the years are discussed.

The authors suggest that the term " follicular lichen planus " most appropriately expresses the clinical and pathological features of the disease.

G. B. Mitchell-Heggs

DERMATITIS

1710. **Treatment of Tinea Capitis with Salicylanilide Preparations**
J. G. HOPKINS, C. S. LINGAMFELTER, M. R. KIESSELBACH, and O. A. HAMILTON. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph. (Chicago)*] **67**, 479–483, May, 1953. 7 refs.

Of 326 patients with tinea capitis who were treated at the Vanderbilt Clinic, New York, during the period 1946–9, the condition was due to infection with *Microsporum audouini* in 263 cases (80%). Two types of ointment, both containing 5% of salicylanilide, were used in treatment, the results of which are analysed in 80 patients who received no other form of treatment. Of 36 patients given the first type of ointment, 15 continued treatment for at least 3 months and of these 4 (27%) were cured; of 19 out of 44 treated with the second type of ointment, 10 (53%) were cured. The authors claim that the cumulative cure rate after 3 months (calculated by actuarial methods) would have been 34% and 63% for the two groups respectively [presumably if all patients had continued with the treatment].

Ten patients who had kerion were also cured without resort to *x*-ray epilation. It is considered that *x*-ray treatment is indicated only if after 3 months the result of examination by Wood light remains positive, for uncooperative patients, and for those with extensive scalp involvement without inflammation. *G. W. Csonka*

1711. **Is Scalp Ringworm in Children a Self-limiting Disease: an Epidemic of Unusually Mild Form Produced by *Microsporum audouini*, Dysgonic Type**
C. H. WHITTLE. *Lancet* [*Lancet*] **2**, 10–12, July 4, 1953. 8 refs.

1712. **Clinical and Histological Observations on the Treatment of Lupus Vulgaris with Isoniazid.** (Documents cliniques et histologiques sur le traitement du lupus tuberculeux par l'hydrazide de l'acide isonicotinique)
P. DE GRACIANSKY, S. BOULLE, M. BOULLE, and J. DALION. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **29**, 1634–1642, May 20, 1953. 14 figs., 16 refs.

The authors describe the good results obtained with isoniazid in the treatment, at the Hôpital Saint-Louis, Paris, of 7 cases of lupus vulgaris in which the duration of the disease ranged from 58 years in one case to 3 months in another. Earlier treatment had been with PAS, large doses of calciferol, streptomycin, surgical curettage, and in one case 800 treatments by Finsen lamp. Treatment with 100 mg. of isoniazid was given 3 times daily for 6 to 10 months, the total dosage varying between 50 and 90 g.; it was supplemented in one case by surgical treatment. Signs of improvement were noted early in the course of treatment, congestion and desquamation soon beginning to decrease. This rendered the lupomata at first more prominent, but 4 to 6 weeks later these underwent a series of characteristic changes in which they first lost their transparent appearance and became opaque and rust-coloured, and then gradually faded, disappearing completely, although they were still perceptible in the skin when examined under compression by a piece of glass.

The results in the series were excellent, 5 patients being completely cured and the remaining 2 showing every sign of imminent cure. One patient underwent curettage of some of his lesions in addition to treatment with isoniazid, and it was noted that the curetted lesions healed in 4 months, the others in 7. There were no toxic effects due to the drug.

From this series the authors conclude that treatment with isoniazid gives quicker results than Charpy's calciferol treatment and that, probably owing to the more rapid rate of healing, there is less dense fibrous scarring and thus a better cosmetic result. Also, in contrast to treatment with calciferol, isoniazid is equally effective in cases involving large and small areas. The histological appearances in biopsy material from these patients are discussed and compared with similar material from calciferol-treated cases. The follow-up period is as yet too short to allow of a final assessment of the method or of any statement concerning the frequency of relapse or the optimum period of treatment.

Ferdinand Hillman

1713. **Treatment of Lupus Vulgaris with Isoniazid. Review of Fifteen Cases**
B. RUSSELL, N. A. THORNE, and R. V. GRANGE. *Lancet* [*Lancet*] **1**, 964–968, May 16, 1953. 2 figs., 14 refs.

As the cure of such a chronic condition as lupus vulgaris can be announced with certainty only after a follow-up period of at least 5 years the authors emphasize that this account of 15 cases of the disease treated at the London Hospital with *iso*nicotinic acid hydrazide (isoniazid) should be regarded as a preliminary report. Of the 15 cases, 12 had received other forms of treatment previously.

Isoniazid was administered either orally (5 cases) or by injection into the lesions (6 cases), or by both methods (4 cases). The most effective oral dosage used was found to be 300 mg. daily and, apart from the development of a mild urticarial rash in one case, there were no undesirable side-effects. For injection into the nodules a solution of 50 mg. (later increased to 100 mg.) in 2 ml. of distilled water was used. Owing to the difficulty for working patients of attending daily, injections were usually made at weekly intervals, a total amount varying from 50 to 250 mg. in 2 to 5 ml. of water being injected into the area each week: daily injection would probably have been more satisfactory. The duration of treatment varied from 10 to 35 weeks.

Although in the time of observation only one patient could be described as clinically cured, all the others except one (whose treatment was interrupted by illness) showed definite improvement of varying degrees. There was no evidence of the organism becoming resistant to isoniazid even after prolonged therapy.

H. R. Vickers

1714. **Contact Dermatitis due to Aminoazotoluene**
R. H. MEARA and I. MARTIN-SCOTT. *British Medical Journal* [*Brit. med. J.*] **1**, 1142–1143, May 23, 1953. 1 fig.

The authors describe 3 cases of contact dermatitis due to the semi-solid inks which are used in a popular ball-pointed pen.

The dermatitis started as a dry, itching, papulo-vesicular eruption on the hands, forearms, and eyelids. The attacks could be related to the use of pens containing red and green ink, but not those with blue ink. It was found that the yellow dye aminoazotoluene was common to both the red and the green ink used in these pens. Controlled patch tests with this dye in 0·01% dilution in yellow soft paraffin gave positive results in all 3 cases. In the first 2 cases epidermal sensitivity to the dye was produced in 6 to 8 weeks, but the interval was longer in the 3rd case. There seems to be an inverse relationship between exposure time and concentration.

Although about 2,000,000 pens filled with red and green ink are sold annually in Britain, these are the only cases reported, and there have not been any cases among the 70 workers exposed to the dye in the manufacture of the inks.

Stephen G. Gang

TUMOURS

1715. **Mycosis Fungoides. Further Report on Cases of Successful Treatment with Antimonials**
J. GARB. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph. (Chicago)*] **67**, 463–466, May, 1953. 6 refs.

Cases have been cited to show the effectiveness of antimonials in some patients with mycosis fungoides, with two of these patients completely free of lesions for four years. It has been emphasized that patients with mycosis fungoides should get a trial administration of antimony potassium tartrate (tartar emetic) injections for six to eight weeks if there are no contraindications, preferably before any other treatment has been used, and, surely, if other treatments failed. Some cases, even with complications, should have a trial administration of stibophen (" fuadin ") alone or alternating with the diethylaminoethanol salt of sodium antimony gluconate (" stibanose ") with a careful watch being kept on the heart, liver, and kidneys.

Although the impression has been gained that patients with tumors and ulcerations of long duration responded best to antimonials, cases have been cited in which patients in the early stages and even a patient with mycosis fungoides *d'emblée* have also responded dramatically to antimonials. For the patients who respond with complete clearing of lesions, antimony treatment is not a palliative method but seems to act as a specific because of the long remissions of about four years in two cases. No less than three injections a week should be given, as infrequent dosage may cause a resistance to antimonials and thus deprive the patient of the only possible chance for recovery. Patients who respond should receive for six months stibophen alone or alternating with the diethylaminoethanol salt of sodium antimony gluconate after all lesions have regressed, possibly to prevent recurrences. For those who feel weak and have loss of appetite following the administration of antimony potassium tartrate the injection should be given two hours after a light supper. Dimenhydrinate (" dramamine ") will also help to control the nausea.—[Author's summary.]

1716. **The Relationship of Molluscum Sebaceum (Kerato-acanthoma) to Spontaneously Healing Epithelioma of the Skin**
F. A. FOURACRES and J. W. WHITTICK. *British Journal of Cancer* [*Brit. J. Cancer*] **7**, 58–64, March, 1953. 5 figs., 13 refs.

Except for a somewhat inaccessible paper by Rook and Whimster (*Arch. belges Derm. Syph.*, 1950, **6**, 137) no adequate description of molluscum sebaceum or kerato-acanthoma—a most interesting lesion—has appeared since the original account given by McCormac and Scarff in 1936 (*Brit. J. Derm.*, **48**, 624). The present authors, in reporting a series of 7 cases from the Royal Cancer Hospital, London, confirm the main features—a nodule growing rapidly in the skin and (in the active phase) histologically closely resembling a small squamous carcinoma, but beginning to regress after about 2 months and ultimately healing entirely. After biopsy with only partial removal of the lesion, their patients were kept under observation without further treatment, their subsequent course demonstrating beyond doubt the very characteristic life cycle of these lesions and showing that there is no ground for considering them to be carcinomata in spite of the histological resemblance.

Other reported cases are discussed, including those described under the diagnosis of " multiple self-healing epithelioma " by Dunn and Smith (*Brit. J. Derm.*, 1934, **46**, 519) which, the authors suggest, were examples of multiple recurrent mollusca sebacea.

Bernard Lennox

The Breast

1717. **Mucous Carcinoma of the Breast. A Systematic Review of 350 Malignant Mammary Epitheliomata.** (Il cancro mucoso della mammella. (Ricerca sistematica su 350 neoplasie epiteliali maligne della mammella))
G. BARBIERI, G. LOTTI, and M. OLIVI. *Lavori dell'Istituto di anatomia e istologia patologica della Università degli Studi di Perugia* [*Lav. Ist. Anat. Univ. Perugia*] **13**, 81–101, 1953. 5 figs., bibliography.

1718. **Adrenalectomy and Oophorectomy in Treatment of Advanced Carcinoma of the Breast**
C. HUGGINS and T. L-Y. DAO. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **151**, 1388–1394, April 18, 1953. 8 figs., 12 refs.

The authors maintain that certain types of cancer arising in tissue which is functionally dependent on hormones are themselves subject to the same influences —that is, their growth can be stimulated or inhibited by the administration of the appropriate hormone. That carcinoma of the breast is a hormone-dependent cancer of this type was first noted in 1896 by Beatson, who reported improvement in 2 cases of cancer of the breast after oophorectomy. However, after removal of the gonads there is compensatory hypertrophy of the adrenal cortex, which takes over the function of secreting oestrogens. If, therefore, it is claimed that carcinoma of the breast can be controlled by the withdrawal of oestrogens, oophorectomy should logically be followed by adrenalectomy, which has become a practical proposition now that adequate substitution therapy is available.

The authors performed adrenalectomy on 55 patients, including 2 men, with advanced carcinoma of the breast during 1951 and 1952. There were 3 operative deaths, all in women, and the 50 remaining cases in women provide the basis of the present survey. All but one had previously been subjected to unilateral or bilateral mastectomy, and all had distant metastases. Half the patients were subjected to adrenalectomy alone, and in the other half oophorectomy was also performed. A measurable decrease in the size or extent of a metastasis, with an improvement in general health and a gain in weight, was regarded as indicative of regression.

The incidence of metastases at various sites and of regression after operation in the 25 patients treated by adrenalectomy alone was as follows:

Site of Metastasis	Incidence	Regression
Bone	20	10
Lung and pleura	7	3
Chest wall	5	2
Area producing oedema of arm	6	1
Lymph nodes	4	2
Intracranial	4	2
Liver	1	1

In the 25 patients subjected to both adrenalectomy and oophorectomy the results were as follows:

Site of Metastasis	Incidence	Regression
Bone	12	8
Lung and pleura	13	5
Chest wall	6	1
Area producing oedema of arm	6	3
Lymph nodes	3	0
Intracranial	1	0
Liver	1	1

Of the 25 women subjected to adrenalectomy alone, 9 died within 7 months of the operation, 3 were alive but with advancing disease at the time of the report, in 10 the disease appeared to have undergone a regression of some magnitude, and in 3 the operation was too recent for evaluation. Among the 25 women subjected to adrenalectomy and oophorectomy there were no post-operative deaths; 8 patients died within 16 months of operation and 3 were alive with evidence of advancing disease; in 4 cases insufficient time had elapsed for evaluation; and in 10 patients there were objective signs of improvement. The follow-up period has so far been short, and it remains to be seen whether regression will be maintained in cases in which it has occurred. As minute osseous metastases occur in many patients with advanced carcinoma of the breast, the serum alkaline-phosphatase level is a good measure of response to this form of treatment; in many of the cases reported a rise in the alkaline-phosphatase level occurred after adrenalectomy, indicating increased osteoblastic activity. A study of the relation between histological type and response to treatment showed that it was only in cases of adenocarcinoma and, to a lesser extent, of papillary carcinoma that regression occurred after adrenalectomy, cases of duct-cell and undifferentiated carcinoma failing to respond.

Discussing the question whether this somewhat formidable procedure is justifiable in patients with advanced malignant disease, the authors state that in the case of the hormone-dependent adenocarcinomata and papillary cancers the mean time of survival after adrenalectomy appears to be significantly longer than can be achieved by the administration of testosterone or oestrogens, and further that adrenalectomy may be effective when there is no response to endocrine therapy.

H. J. B. Atkins

1719. **Recurrences and Metastases in Cancer of the Breast. An Analysis of One Hundred Cases**
P. W. HOFFERT and E. P. PENDERGRASS. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **70**, 376–386, Sept., 1953. 5 figs., 15 refs.

Paediatrics

1720. **Blood Glucose Changes in the Newborn. 1. The Blood Glucose Pattern of Normal Infants in the First 12 Hours of Life**
R. D. G. CREERY and T. J. PARKINSON. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **28**, 134–139, April, 1953. 3 figs., 10 refs.

In 46 cases of normal birth at Southmead Hospital, Bristol, the blood glucose level was determined in both mother and newborn infant (23 males and 23 females). Criteria for normality were: (1) mother not anaesthetized and having received only analgesics having no effect on blood glucose; (2) spontaneous vertex delivery of the infant at full term; (3) no asphyxia in the baby, and regular breathing established within 3 minutes; (4) no observed abnormality of temperature, pulse rate, or breathing; (5) no sign of cerebral damage; and (6) no development of clinical abnormality which could be attributed to birth trauma. The blood glucose content was estimated by the method of King and Garner. The first blood sample was taken from the mother's ear at the moment of crowning of the foetal head, the second from the infant's umbilical vein (in a few cases from the umbilical artery), and thereafter the samples, consisting of 0·05 ml. of blood, were taken from the infant's heel at 30-minute intervals for the first 3 hours, and then at 3-hourly intervals for the next 9 hours of life. No fluid or feed was given to the infant for the first 3 hours, and later samples were taken immediately before a feed was due.

There was wide variation in the range of glucose values, but the scatter lessened progressively during the 12-hour period. There was no difference between the values in male and female infants. During the first hour after delivery the mean glucose concentration in the infants' blood fell from 79 mg. per 100 ml. to 53 mg. per 100 ml., and this level was maintained. It is concluded that the normal range of blood glucose values for babies in the first 12 hours of life may be taken to vary from 30 to 75 mg. per 100 ml. No correlation between birth weight and blood glucose values was observed.

E. H. Johnson

1721. **Coeliac Disease. III. Excretion of Unsaturated and Saturated Fatty Acids by Patients with Coeliac Disease.** [In English]
H. A. WEIJERS and J. H. VAN DE KAMER. *Acta paediatrica* [*Acta paediat. (Uppsala)*] **42**, 97–112, March, 1953. 14 figs., 8 refs.

In this investigation, carried out at the Children's Hospital and the Central Institute for Nutrition Research, Utrecht, the faeces of children with coeliac disease were shown to contain a higher proportion of saturated than unsaturated fats. The administration of a less saturated fat (in the form of olive oil) resulted in an apparent improvement in absorption. When wheat gluten was present in the diet the amount of saturated fat in the faeces was increased, and in some cases exceeded the saturated fatty acid content of the diet. It was not considered that intestinal flora could be responsible for this high content of non-dietary saturated fatty acid, since it continued in spite of administration for 6 days of streptomycin. The authors conclude that there is some unexplained failure in intermediary lipid metabolism in coeliac disease. *A. C. Frazer*

1722. **On Psychogenic Obesity in Children. II.** [In English]
N. JUEL-NIELSEN. *Acta paediatrica* [*Acta paediat. (Uppsala)*] **42**, 130–146, March, 1953.

The author reports the results of re-examination of 61 children (36 girls and 25 boys) under treatment for obesity at the Kommunehospital, Aarhus, Denmark; the procedures and approach originally described by Bruch were employed. There was little sign of any characteristic psychological or social pattern in the environment of these children such as Bruch stated to be typical for the obese child. Obesity was associated with increased food intake and reduced activity in most cases. Of the 61 cases examined, only 9 could be diagnosed as psychogenic with reasonable certainty, and of these only 3 presented the characteristic family pattern and psychogenic mechanisms described by Bruch. In 40 of the cases there was definitely no evidence of significant psychogenic factors. *A. C. Frazer*

1723. **Hematologic Adjustments to Cyanotic Congenital Heart Disease**
A. M. RUDOLPH, A. S. NADAS, and W. H. BORGES. *Pediatrics* [*Pediatrics*] **11**, 454–464, May, 1953. 9 figs., 5 refs.

The authors have recently observed several cases of children with cyanotic congenital heart disease who were found to have polycythaemia with a haemoglobin level within the normal range for their age, and therefore low in proportion to the number of erythrocytes. This condition, which the authors call "relative anaemia", responds rapidly to treatment with iron. Not only does the haemoglobin value rise, but the patients' irritability, anorexia, poor weight gain, dyspnoea, and cyanotic attacks are alleviated. Symptoms recur, however, when the haematocrit reading rises above 70 to 75%, and this is thought to be due to the rapid increases in blood viscosity which occur at these high haematocrit levels.

In an attempt to explain the mechanism of the relative anaemia, a group of 7 children aged 5 months to 4 years with congenital heart disease were studied at the Children's Medical Center (Harvard Medical School), Boston, for their response to iron in the form of ferrous sulphate. Children with little or no cyanosis showed the usual

decrease in erythrocytes and haemoglobin level a few months after birth. In the more severely cyanotic infants on the other hand there was no initial fall, polycythaemia occurred early, and later the haemoglobin level declined, so that by the age of 9 months there was a relative anaemia. It appears that the normal postnatal fall in haemoglobin value and erythrocyte count is due not to iron deficiency but to a rise in oxygen tension. If anoxia is present, as in cyanotic heart disease, the number of erythrocytes is maintained at a high level, requiring large intake of iron, both prenatal and dietary, if relative anaemia is not to develop. The practice of maintaining a high fluid intake in these patients to prevent dehydration will aggravate the iron deficiency, and solid feeding should be started early. It is stressed in conclusion that the finding of a " normal " haemoglobin level in children with cyanotic congenital heart disease is not sufficient evidence of absence of anaemia.

A. Paton

1724. **Acute Epiglottitis (Acute Supraglottitis)**
F. E. CAMPS. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **46**, 281–284, April, 1953. 3 figs., 10 refs.

This paper draws attention to a severe infective condition, the occurrence of which in young children has (since 1941) been more generally recognized in the U.S.A. than elsewhere, consisting in an acute localized infection of the epiglottis due to *Haemophilus influenzae* Type B and causing respiratory obstruction. Its importance lies in the fact that death is almost inevitable unless an early diagnosis is made and prompt and vigorous antibacterial treatment given. Tracheotomy may be necessary, but intubation is contraindicated as pressure on the infected tissues contributes to the persistence of bacteraemia. Hitherto only one case had been reported in Great Britain (De Navasquez, *Brit. med. J.*, 1942, **2**, 187) although there is strong evidence that a number of fatal cases have in fact occurred since 1944, but have not been described in the literature. [The abstracter has knowledge of several such cases, details of which were communicated privately to him.]

The present author reports 19 cases of acute epiglottitis seen at necropsy since 1944. The age incidence was from 9 months to 5½ years, the maximum number of cases occurring between the 3rd and 5th years. All but one case occurred between September and March. The clinical picture was fairly clear-cut and showed the following features: (1) acute onset with pyrexia of 104° to 106° F. (40° to 41° C.), sore throat, difficulty in swallowing, and restlessness; (2) no obvious nasopharyngitis; (3) respiratory obstruction with expiratory stridor, grey-white cyanosis, rib recession, and swollen epiglottis; and (4) sudden collapse associated with acute laryngeal obstruction 9½ to 48 hours after onset, and rapid death, sometimes with terminal convulsions.

Pathological changes in the author's cases were virtually confined to the region of the epiglottis, which showed a brawny, red oedema without involvement of the true vocal cords or tonsils. In one case *H. influenzae* Type B was isolated from the epiglottis and in another *H. influenzae* was isolated but not typed. According to American reports this organism has frequently been identified in the local lesion and in blood cultures during life, and it was also identified by De Navasquez in his original case. It seems probable, therefore, that the aetiology of the disease in Britain is the same as in America, and the author suggests that more attention should be paid to the presence of *H. influenzae* Type B in the routine examination of throat swabs from children. As regards treatment, good results have been reported by American authors with aureomycin, chloramphenicol, penicillin and, on occasion, rabbit antiserum to *H. influenzae* Type B. [Tests carried out by the abstracter (a report of which is at present in the press) on a considerable number of capsulated type-specific and non-capsulated strains of *H. influenzae in vitro* show chloramphenicol to be much superior to all the other commonly available antibiotics in its effect on this organism. In acute epiglottitis 3 to 4 days' intensive treatment with chloramphenicol would probably be sufficient, and the risk of aplastic anaemia (which may occur in 4 to 5% of cases treated over long periods with this drug) therefore small compared with the risk of a fatal issue if treatment is inadequate.]

A useful table is appended giving the points of differential diagnosis between acute epiglottitis and acute laryngo-tracheobronchitis. *K. S. Zinnemann*

1725. **The Diagnosis of Acute Meningitis in Infancy**
J. C. HAWORTH. *Lancet* [*Lancet*] **1**, 911–914, May 9, 1953. 12 refs.

The author has analysed the case records of 50 infants under the age of 12 months admitted to Alder Hey Children's Hospital, Liverpool, with acute purulent meningitis. The infection was due to meningococcus in 24 cases, pneumococcus in 5, *Bacterium coli* in 5, and *Haemophilus influenzae* in 4; in 12 no organism was isolated. Details of 6 of the cases are given in full.

Of the 50 cases, 13 showed none of the clinical signs of meningitis; there was no neck rigidity, bulging of the fontanelles, or positive Kernig's sign. In 7 of these 13 cases the patient died.

The difficulties in diagnosis are emphasized, and it is suggested that lumbar puncture should be performed on every infant: (1) who is unusually drowsy or irritable, or has a " vacant look " or a recent squint; (2) who is more ill than can be explained by the physical signs; or (3) who does not make the expected response to treatment for such a disease as pneumonia or gastroenteritis. Furthermore, the classical signs of meningitis should not be awaited before lumbar puncture is performed, because these signs develop only late in the disease in a high proportion of cases.

Five babies had convulsions at the onset and 9 developed convulsions after admission; 8 of these 14 died (mortality 57%) and one developed hydrocephalus and spasticity. Of the 36 in whom fits did not occur, only 3 died (mortality 8%). The author suggests that in the meningitis of infants and small children anticonvulsant drugs should be used as a routine, because of the bad prognosis when fits occur. *R. S. Illingworth*

Public Health and Industrial Medicine

1726. **The 1952 Encephalitis Outbreak in California**
W. L. HALVERSON, W. A. LONGSHORE, and R. F. PETERS. *Public Health Reports* [*Publ. Hlth Rep.* (*Wash.*)] **68**, 369–377, April, 1953. 16 figs.

Human infection with Western equine encephalomyelitis virus in California was first identified in pathological specimens in 1932 and confirmed by isolation of the virus in 1938. During the period 1938–51 the number of cases of infectious encephalitis varied widely, the incidence of the disease being highest in 1945 and 1950, when 320 and 357 cases were reported respectively. In 1952, however, there were 729 cases, with 51 deaths. Although these cases were reported from 37 of the 58 counties in the State, 94% (689) occurred in the 20 counties of the Central Valley, where unusual meteorological conditions proved exceptionally favourable for the multiplication and spread of the insect vector *Culex tarsalis*. This mosquito is resistant to DDT and other chlorinated hydrocarbons.

The present paper is a preliminary report, from the California State Department of Public Health, of the emergency measures which were developed to deal with the epidemic, and of the research which was carried out into the epidemiology of the two infecting organisms, namely, the virus of Western equine encephalitis and the virus of St. Louis encephalitis. The emergency plans called for the cooperation of Federal and State agencies with local health departments, the full help of the State virus laboratory and of private practitioners and local hospitals, and the mobilization of all mosquito-control agencies. The authors briefly describe the steps that were taken as soon as the incidence of cases began to rise and an epidemic was expected, the administrative problems encountered, the State and Federal aid given, the epidemiological investigations, and the mosquito-control measures.

A later report is promised [and this will presumably state more clearly whether one, or more than one, specific virus was involved in this outbreak]. *J. Cauchi*

1727. **An Outbreak of Diphtheria: Influence of Immunization**
C. D. L. LYCETT and J. T. A. GEORGE. *British Medical Journal* [*Brit. med. J.*] **1**, 964–968, May 2, 1953. 2 figs., 5 refs.

In an outbreak of diphtheria in 1951 affecting a number of districts in the Administrative County of Stafford with a total population of 267,250 there were 108 confirmed cases with 6 deaths. These 108 cases represented 15·4% of the 699 provisional corrected notifications for England and Wales in that year. In spite of an apparently satisfactory immunization programme this district showed an unusual incidence of cases of diphtheria in recent years and a change in type of *Corynebacterium diphtheriae* from *mitis* and *intermedius* to *gravis*. The last outbreak was most probably due to a low level of immunity of the child population and not to the exclusive occurrence of the *gravis* type of diphtheria. The majority of cases (65·7%) occurred in children of school age. The authors emphasize the importance of frequent re-immunization.
Franz Heimann

INDUSTRIAL MEDICINE

1728. **Cholinesterase Response and Symptomatology from Exposure to Organic Phosphorus Insecticides**
W. T. SUMERFORD, W. J. HAYES, J. M. JOHNSTON, K. WALKER, and J. SPILLANE. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg.*] **7**, 383–398, May, 1953. 2 figs., 9 refs.

A study was carried out by the U.S. Public Health Service of the cholinesterase activity of the blood in relation to symptoms of illness in 258 persons living in the fruit-growing area of Wenatchee, Washington, who were exposed in varying degree to the organo-phosphorus insecticides "parathion" and tetraethylpyrophosphate (TEPP). The subjects included spray mixers and sprayers, who were the most heavily exposed, orchard workers and warehousemen, residents living near the orchards but with no occupational contact with the insecticides, and residents living at some distance from the orchards, in whom the possibility of minimal exposure could not be excluded. A control group of persons living outside the area was also included.

The average cholinesterase value (ΔpH per hour) of the erythrocytes in the control group was 0·72 and of the plasma 0·91, the corresponding values for pre-exposure samples taken in Wenatchee being 0·77 and 0·88. During the period of exposure the average values in all groups definitely in contact with the insecticides were reduced and the incidence of illnesses suggestive of poisoning was increased. However, symptoms of mild illness were present in many persons while their blood cholinesterase activity was within the normal range, although it may have fallen below the normal for the individual. [Barnes (*Wld Hlth Org. techn. Rep. Ser.*, 1953, No. 16, 64) states to the contrary that "the blood cholinesterase level always falls to less than one-fifth of its normal activity before symptoms are noticed".] On the other hand prolonged exposure to organo-phosphorus insecticides was capable of gradually reducing the cholinesterase activity of the blood to a very low level (0·11 in one case) without any symptoms of illness developing. It follows that a blood cholinesterase estimation during exposure is of little diagnostic value unless it can be compared with the pre-exposure value for that individual. In every case of severe poisoning, however, the onset of symptoms was accompanied by a depression of blood cholinesterase activity, the rapidity of the fall being more

closely related to the severity of the symptoms than its extent. Serious poisoning resulted in every case from a severe, brief exposure. The extent of the depression of blood cholinesterase activity in any individual or group of persons was found to be correlated with the degree of exposure and to be an index of the need for improvement in safety precautions.

Organo-phosphorus poisoning was considered to be likely in the presence of myosis or at least three of the following symptoms (listed in order of frequency): headache, nausea, weakness or fatigue, pain or tightness in the chest, abdominal pain, vertigo, fainting or incoordination, vomiting, nervousness, drowsiness or insomnia, sweating, cough or expectoration, disturbances of vision, loss of appetite, shortness of breath, nasal discharge, and wheeze. A significant fall in the blood cholinesterase level in such cases was regarded as diagnostic. Myosis was present in only 5 out of 38 cases which fulfilled the above criteria, and 2 of these patients had no disturbance of vision. Eye symptoms were attributed by the workers more often to TEPP than to parathion. *M. A. Dobbin Crawford*

1729. **Paralysis following Poisoning by a New Organic Phosphorus Insecticide (Mipafox). Report on Two Cases**
P. L. Bidstrup, J. A. Bonnell, and A. G. Beckett. *British Medical Journal* [*Brit. med. J.*] **1**, 1068–1072, May 16, 1953. 3 figs., 19 refs.

Mipafox (bis-(mono-*iso*propylamino)-fluorophosphine oxide) is a new organic phosphorus compound which, in common with other compounds of this type, inhibits cholinesterase activity *in vitro* and *in vivo*. It has been shown to possess only one-twenty-sixth of the toxicity of "parathion" for rabbits and guinea-pigs, but 3 cases of poisoning with mipafox have occurred among workers engaged in its manufacture. These cases, which are described in this paper, showed the usual acute symptoms characteristic of poisoning by an organic phosphorus compound.

Of the 3 patients, 2 developed paralysis about 2 weeks after the acute illness; in both cases there was a previous history of attacks of mild poisoning by organic phosphorus compounds. In the third case there was no such history, and mild acute symptoms but not paralysis developed. In the 2 complicated cases flaccid paralysis developed, involving both arms and legs in one case and mainly the legs in the other. Reflexes were reduced or absent, but there were no sensory changes apart from muscle tenderness. Muscle twitching was seen in the face, deltoid, and leg muscles. Wasting developed in the paralysed muscles, particularly the small muscles of the hands and feet. These symptoms reached their peak about 4 weeks after their first appearance, and then showed gradual improvement which progressed for many months, but had not resulted in full recovery at the time of the report [presumably about 18 months after the onset of paralysis].

The history of these cases and those reported elsewhere in the literature suggests that repeated exposure to cholinesterase inhibitors may be one of the factors causing paralysis. Experimental results reported in this paper show that the plasma cholinesterase level recovers more slowly after poisoning by mipafox than after that caused by tetraethylpyrophosphate (TEPP) and di-*iso*-propylfluorophosphonate (DFP). Thus the state of increased sensitivity to the effects of anticholinesterase agents which follows poisoning by one of them will be prolonged after poisoning by mipafox.

Earl and Thompson (*Brit. J. Pharmacol.*, 1952, **7**, 685) have shown that reduction in pseudo-cholinesterase level in animals results in demyelination in the central nervous system and peripheral nerves, and it is possible that this mechanism may account for the persistent signs and symptoms of peripheral neuritis in the 2 cases described in the present paper.

Electromyographic studies of the first patient gave results comparable with those found when the motor end-plate is progressively depolarized after the administration of decamethonium iodide, while further observations 8 months after the onset of paralysis were indicative of peripheral neuritis. Therefore the paralysis in the early stages, which occurred after moderate exertion, may have been due to failure of transmission of the nerve impulse at the motor end-plate.

It was noted that muscular hypotonia may occur apart from other signs and symptoms when cholinesterase activity is reduced, and it is suggested that this sign should be sought during convalescence from acute poisoning, when its presence may indicate that the plasma cholinesterase level is still low and that the period of rest should be prolonged. *W. K. S. Moore*

1730. **Disability due to Inhalation of Grain Dust**
V. L. Cohen and H. Osgood. *Journal of Allergy* [*J. Allergy*] **24**, 193–211, May, 1953. 7 figs., 4 refs.

The authors describe 11 cases in which the patients were suffering from symptoms due to the inhalation of crude grain dust over many years. The average age of the patients was 56 years, and they had been exposed to dust in grain elevators and animal feeding-stuff mills for an average of 27 years. Their symptoms had started some 6 years previously and had increased gradually. All suffered from dyspnoea, and many from cough and wheezing. Most of them had emphysema and showed a reduced vital capacity. Radiologically, there was no evidence of silicosis or other nodulation. Intradermal skin testing gave a positive reaction to crude grain dust in 6 patients, and these 6 patients were also sensitive to other allergens such as pollen, foods, or common inhalants. Of the total of 11 patients, 4 died while under observation, necropsy being performed on 3 of them. This revealed the presence of carcinoma in 2 and of lobar pneumonia in the third; all 3 of them had emphysema and cor pulmonale.

The authors are [rightly, in the abstracter's opinion] doubtful whether the development of allergic sensitivity in these "grain handlers" had caused the disabling disease or whether the purely irritative effect of grain dust inhaled over long periods was responsible for the disabling respiratory symptoms. *H. Herxheimer*

See also Pathology, Abstract 1483.

Anaesthetics

1731. **Controlled Hypotension in Neurosurgery with Hexamethonium and Procaine Amide**
D. ASERMAN. *British Medical Journal* [*Brit. med. J.*] **1**, 961–964, May 2, 1953. 3 refs.

This paper from the National Hospital, Queen Square, London, is based on a study of 90 cases in which hypotension was induced for surgery of the brain. The known dangers, such as liver damage, tissue anoxia, thrombosis, and reactionary haemorrhage, of hypotensive anaesthesia are recalled, and a new danger, which the author has called " retractor anaemia ", is discussed at some length. When hypotension is induced, the brain shrinks, its consistency is altered, it loses elasticity, and behaves like soft dough. In this condition it is easily deformed by pressure and is slow to regain its normal contour on release; blood is forced out of the parts of the brain subjected to pressure, and because of the reduced blood flow the vessels are slow to refill when the pressure is removed. Large areas of brain may thus be rendered anaemic by the pressure of the brain-retractor and may be irreversibly damaged. The author records 3 cases of death after craniotomy under hypotensive anaesthesia. In each case the cerebral hemisphere on the operated side was greatly enlarged by oedema, and this was attributed to vascular damage due to anaemia caused by pressure of the retractor.

In this series, when hexamethonium bromide was the only hypotensive drug used, failure to achieve a satisfactory fall in blood pressure occurred in about 40% of the cases. When, however, procaineamide was used in addition in those cases which did not respond to hexamethonium alone, the failure rate was reduced to 15%. Procaineamide should be given by the slow intravenous injection of from 200 to 500 mg. of the drug when it is apparent that a satisfactory fall will not be achieved or maintained by the first dose of hexamethonium. The duration of the effect of this combination of drugs is unpredictable, but if the blood pressure rises, a second dose of procaineamide, " much smaller than the first ", is given. *Ronald Woolmer*

1732. **Controlled Hypotension in Neurosurgery.** (L'hypotension contrôlée en neuro-chirurgie)
D. PETIT-DUTAILLIS and G. GUIOT. *Mémoires de l'Académie de chirurgie* [*Mém. Acad. Chir. (Paris)*] **79**, 373–376, May 6–13, 1953.

After first using hexamethonium as a hypotensive agent, the authors now prefer " pendiomide " (azamethonium bromide) owing to its complete lack of toxicity and its generally satisfactory effect. Stress is laid on the importance of test dosage and of making alterations in posture very gradually, taking 15 to 20 minutes to change from the supine to the sitting position. For the purposes of intracranial surgery it is advisable, in the authors' opinion, to restrict the time of administration of the drug to the interval between raising the bone flap and entering the dural space.

In their series of 160 cases severe complications have rarely been met and lesser ones, such as undue cerebral ischaemia and excessive prolongation of the action of the drug, were readily combated by change of posture. There have been no cases of coronary thrombosis and no increase in the incidence of postoperative cerebral thrombosis.

The authors eschew the use of controlled hypotension as a routine for neurosurgery, and must be convinced of the likelihood of its increasing the chances of recovery before employing it. They rarely use it for patients over the age of 60, and never in the presence of arteriosclerosis or angina. The procedure has given best results in the excision of very haemorrhagic tumours and aneurysms. Hypertension is not regarded as a contraindication, but careful preparation, with intramuscular injections of pentamethonium for 24 to 48 hours before operation, is essential.

Of the 160 operations in which the technique was used, 121 were for the excision of tumours. There were 27 deaths in the whole series (16%). The operative mortality in cases of cerebral tumour was 14%, which compares very favourably with their previous figure of 25%. The operative mortality in cases of glioma has been reduced from 28 to 10·5% and that in cases of meningioma from 35 to 10·8%.

A further valuable use for the hypotensive drugs is in the treatment of the acute cerebral oedema which occurs so often after operations on the posterior fossa or even after simple ventricular puncture, and which has hitherto always been irreversible and rapidly fatal. Recovery from this condition occurs rapidly after administration of a hypotensive agent. *Michael Kerr*

1733. **Controlled Hypotension in General Surgery.** (L'hypotension contrôlée en chirurgie générale)
A. SICARD and Y. SIBAUD. *Mémoires de l'Académie de chirurgie* [*Mém. Acad. Chir. (Paris)*] **79**, 361–368, May 6–13, 1953.

The authors describe their experience of controlled hypotension for general surgery, which they have used in 125 cases, the patients' ages ranging from 3 to 83 years. Pentamethonium was the only agent employed, and the operations performed included such simple procedures as tendon suture in order that the value of controlled hypotension might be assessed over as wide a range as possible.

The reduction of haemorrhage was excellent in 107 cases and inadequate or absent in 18. There were 2 fatal cases, the first that of a fat woman of 62 who was placed in the prone position for exploration of a cervical intervertebral disk. [No details are given of the anaesthetic technique apart from the dosage of pentamethonium

which was 50 mg.] The blood pressure fell to 40 mm. Hg and cyanosis supervened in spite of assisted respiration; shortly after this, cardiac arrest occurred. The authors blame the obesity of the patient and the posture on the table for the fatal state of anoxia. The second fatality occurred during cervical sympathectomy in a girl of 19 who likewise exhibited severe cyanosis 45 minutes after the start of the operation. This was unhappily relieved too late and death eventually occurred after 3 days in a vegetative state. The authors consider this to have been the result of prolonged cardiac arrest [but there is also passing mention of an interruption in the oxygen supply owing to exhaustion of a cylinder].

In summarizing their experience the authors stress the importance of avoidance of anoxia, light premedication, and minimum movement of the patient. Definite contraindications are hypertension, atheroma or other arterial disease, and a past history of coronary or cerebral ischemia or renal deficiency.

(During the subsequent discussion stress was laid on the importance of maintaining a minimum systolic pressure of 40 mm. Hg, as the methonium salts are not metabolized, but are excreted by the kidney.)

Michael Kerr

1734. **The Results of Two Years' Experience of Controlled Hypotension.** (Bilan de deux années d'expérience de l'hypotension contrôlée)

R. MERLE D'AUBIGNÉ and E. KERN. *Mémoires de l'Académie de chirurgie* [*Mém. Acad. Chir.* (*Paris*)] **79**, 368–373, May 6–13, 1953.

The authors present an analysis of 300 cases in which they have used controlled hypotension for orthopaedic operations during the past 2 years. Operations about the hip-joint accounted for just over one-third of the cases and vertebral interventions for just under one-third, the remainder of the operations being equally divided between the head and neck and extremities. The results were good in 223 cases and poor in 45, and in 32 there was complete failure to produce a bloodless field. The importance of adequate postural drainage is emphasized and orthopaedic tables are condemned as unsuitable for this technique. However, in many cases failure occurs without obvious cause, and an adequate reserve of blood should be available in case it should be required.

The indications for controlled hypotension are divided into two main groups—operations in which severe blood loss is liable to occur, and those in which operative success may be jeopardized by a bloody field. Apart from dangers arising from the indiscriminate and insufficiently skilful use of the technique, its chief drawbacks are the possibility of ischaemic complications and of the occurrence of postoperative haemorrhage or thrombosis. While the authors have experienced no case of cerebral ischaemic complications, and postoperative haemorrhage has not been encountered with increased frequency, they regard coronary thrombosis as undoubtedly the commonest cause of death associated with controlled hypotension, and the utmost care in preoperative evaluation of coronary efficiency is advised. In thoracic surgery the inversion of intrathoracic pressures occasioned by controlled or assisted respiration, with consequent diminution in venous return to the heart, is held responsible for the high incidence of complications of hypotensive procedures reported by some authorities; moreover, it is theoretically undesirable to depress the circulatory system when respiratory function is already disturbed. Renal complications have not been met and are considered only as a theoretical possibility.

Michael Kerr

1735. **A Survey of 92 Cases of Hibernation.** (Réflexions à propos de 92 cas d'hibernation)

J. HEPP and R. ALLUAUME. *Mémoires de l'Académie de chirurgie* [*Mém. Acad. Chir.* (*Paris*)] **79**, 381–387, May 6–13, 1953.

The greater part of this paper is devoted to a discussion of basic principles and a description of the development of the authors' technique of refrigeration anaesthesia or artificial hibernation during the past 18 months. The points upon which greatest emphasis is laid concern the lowered anaesthetic resistance of the hypothermic patient and the need for control of the supervening hypotension, avoidance of anuria and decerebration, and reduction of fluid intake to avoid overloading the depressed circulation.

The remainder of the paper gives some indication of the procedures for which refrigeration anaesthesia has been used and the results. Of the 92 patients in the authors' series, 16 died, but in no case was death attributable to refrigeration. There were 30 cases of major abdominal surgery by the thoracic approach and 26 by the abdominal route, and practically all cases involved heroic surgery on a patient *in extremis*. Excellent results are reported in operations on the biliary tract and pancreas, especially when jaundice was present, and in cardiac surgery. Great stress is laid upon the necessity for continuous and stringent supervision throughout.

Michael Kerr

1736. **Circulatory Effects of Prolonged Light Anaesthesia in Man**

G. DE J. LEE, H. CHURCHILL-DAVIDSON, B. E. MILES, and H. E. DE WARDENER. *Clinical Science* [*Clin. Sci.*] **12**, 169–174, May, 1953. 2 figs., 13 refs.

In this paper are reported the results of a study made at St. Thomas's Hospital, London, of the cardiac output, pulse rate, forearm blood flow, blood pressure, renal blood flow, glomerular filtration rate, and intrathoracic blood volume in 6 healthy male patients studied before and during extensive operations for varicose veins under light anaesthesia maintained for 2½ hours with cyclopropane and oxygen in a closed circuit. Details are given of the tests used, and the results of each test in the 6 subjects are presented in a composite chart.

Cardiac output fell early by about 21%, and as anaesthesia continued there was a further fall. The forearm blood flow rose by about 24% early in anaesthesia, indicating dilatation of the blood vessels of the muscles, and then descended to a value just above that for conscious normal subjects. The pulse rate and mean blood

pressure were slightly lowered, but the blood pressure returned nearly to normal levels as anaesthesia was continued. Renal blood flow (measured by clearance of inulin and PAH) fell at first to little more than half the control value, and although it rose again slightly as anaesthesia was continued, in no case did it return to normal for the 2½ hours of the experiment. The effect on the glomerular filtration rate was similar. The intrathoracic blood volume—measured by the dye technique described by Hamilton *et al.* (*Amer. J. Physiol.*, 1948, **153**, 309)—was normal at first, but decreased by about 12% during the subsequent 2 hours.

Thus it appears that under this form of anaesthesia there is at first a diminished cardiac output with vasoconstriction of the renal vessels and vasodilatation in the muscles. As anaesthesia continues the tone of the muscle vasculature returns towards normal, thus raising the peripheral resistance, so that the blood pressure is maintained in spite of a falling cardiac output. The initial fall in cardiac output and blood pressure is contrary to the findings of other workers, but the authors suggest that this discrepancy may have been due to the depth of anaesthesia employed, which in this study was light enough to allow occasional reflex muscular activity to occur. *Ronald Woolmer*

1737. **Circulatory Effects of Haemorrhage during Prolonged Light Anaesthesia in Man**
H. E. DE WARDENER, B. E. MILES, G. DE J. LEE, H. CHURCHILL-DAVIDSON, D. WYLIE, and E. P. SHARPEY-SCHAFER. *Clinical Science* [*Clin. Sci.*] **12**, 175–184, May, 1953. 3 figs., 14 refs.

In this further study [see Abstract 1736] carried out at St. Thomas's Hospital, London, 14 healthy male patients undergoing operation for varicose veins were subjected to venesection under light general anaesthesia, the anaesthetic agent being ether in 3 cases and cyclopropane in 11 cases. About one-quarter of the patient's total blood volume was withdrawn quickly and subsequently replaced. Changes in the muscle blood flow, renal blood flow, cardiac output, intrathoracic blood volume, blood pressure, and pulse rate were observed, and are presented in tabular and graphic form.

An important contrast was apparent between the response to rapid blood loss in the conscious and in the anaesthetized subject. In most conscious subjects it resulted in dilatation of the muscle vessels and vasovagal fainting: in anaesthetized subjects it resulted in constriction of the muscle vessels. It is suggested that this reaction is responsible for the reduction in bleeding during surgery, since it reverses the vasodilatation which is otherwise produced by anaesthesia.

The renal blood flow and the glomerular filtration rate showed no significant change. It is evident, therefore, that the renal vessels do not constrict as do the muscle vessels, but tend rather to dilate. The cardiac output fell markedly as a result of the venesection. The fall was of the order of 33%, and was steeper and more profound than the fall previously shown by the authors to occur under anaesthesia without haemorrhage. The pulse rate and the blood pressure (except in 2 cases) showed remarkably little change, in spite of an oligaemia amounting to one-quarter of the blood volume. It is apparent, therefore, that severe oligaemia may be unrecognized if these two measurements only are used as a guide. The mean circulation time was increased in all cases after venesection. There was a fall in the intrathoracic blood volume, suggesting that a transfer of some of the blood from the pulmonary circulation takes place in response to haemorrhage. *Ronald Woolmer*

1738. **Studies on Venous Blood Pressure in Patients undergoing Major Surgical Procedures**
V. K. PIERCE, C. P. BOYAN, and J. G. MASTERSON. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **96**, 310–314, March, 1953. 4 figs., 3 refs.

A fall in arterial pressure is regarded as an index to the degree of shock. In very radical surgery, however, there may be considerable blood loss which, for a brief period, may not be reflected in the systolic readings. Then, if replacement has not been prompt, the pressure may fall, even to zero. In the experimental animal Moon has shown that in shock low venous pressure usually precedes the fall in arterial pressure. Venous pressure is very variable in different veins. It is influenced by position as well as by medication, anaesthesia, and operation. Comparison must, therefore, be limited to values in any one vein of the patient; basic readings are determined after anaesthesia is induced and positioning completed.

In order to detect reduction in blood volume (that is, impending shock) before the fall in arterial pressure, studies were carried out on venous pressure in 60 patients undergoing major surgery at the Memorial Center for Cancer and Allied Diseases, New York. All the patients, whose ages ranged from 12 to 73 years, received the same type of anaesthesia. Pre- and post-operative determinations of blood volume were made. A saline manometer was introduced into the intravenous-drip system. Used swabs and sponges were weighed to estimate the blood loss. Arterial and venous pressures were noted with the patient in various positions. Deepening the anaesthesia or the insertion of abdominal packs caused a decrease in venous pressure; it was raised by exploration of the abdomen and traction on the viscera.

In all cases associated with blood loss there was a significant fall in venous pressure if the blood was not replaced; this preceded the fall in arterial pressure and the increase in pulse rate. The loss required to produce significant changes varied, being less in those whose preoperative blood volume was low. This fact is considered to demonstrate the labile status of patients with " chronic shock "—that is, those with diminished blood volume. These patients usually have a normal arterial pressure and pulse rate and show no clinical evidence of shock. It is suggested that the method may be very valuable in these cases. Venous pressure readings also appeared to give a more accurate index of a return to normal after post-haemorrhagic blood replacement. Fatal overtransfusion due to reliance upon arterial pressure readings may be prevented by using venous pressure readings.
W. Stanley Sykes

Radiology

1739. **The Treatment of the After-effects of *X*-irradiation with Dihydroergotamine.** (Die Behandlung des Röntgenkaters mit Dihydroergotamin)
K. WERNER. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **83**, 431–432, May 2, 1953. 22 refs.

The fact that a great number and variety of remedies for the relief of radiation sickness have been suggested and employed in the past has convinced the author that the mechanism underlying this condition is both very complex in nature and, so far, but little understood. He believes that the radiation syndrome occurs as the result of "a direct radiation effect on the body's neuro-glandular system, which in turn affects its vegetative behaviour"; to this must be added the reaction of the organism to radiation-induced tissue changes.

In searching for an antidote at the Czerny Hospital (University of Heidelberg) the author stumbled upon dihydroergotamine 45. A dose of 10 to 20 drops of a solution containing 1 mg. of dihydroergotamine per ml. was given 3 times daily before meals to a total of 210 patients suffering from untoward radiation effects. Marked and almost instantaneous relief was obtained in 169 of these, relief in 14 after some time; 8 were considerably improved, and 19 were not benefited. These favourable results are compared with those of other drugs. *Jan G. de Winter*

RADIODIAGNOSIS

1740. **Diagnostic Radiological Aspects of Hypopharyngeal Cancer**
W. WELIN. *British Journal of Radiology* [*Brit. J. Radiol.*] 26, 218–223, May, 1953. 10 figs.

This paper is based on an extensive experience of the radiological diagnosis of carcinoma of the hypopharynx at the Karolinska Hospital, Stockholm, where no fewer than 510 cases of hypopharyngeal cancer have been seen since the hospital was opened in February, 1940. The frequency of this condition according to site and sex is discussed and mention made of the Plummer–Vinson syndrome, which the author regards as precancerous. It is pointed out that the main purpose of radiology in cases of carcinoma of the upper portion of the hypopharynx is to help define the extent of the tumour, whereas when the lower portion is affected the procedure is primarily diagnostic.

In describing technique, emphasis is given to the taking of films after coating the mucosa with a barium suspension of creamy consistency (good-quality radiographs being reproduced to illustrate the value of this method). In cases of Plummer–Vinson syndrome radiographs are taken with maximum filling in order to detect possible web formation, and follow-up examinations are carried out at intervals of 6 months. It is suggested that post-radiation changes should be distinguished from recurrence of neoplasm by biopsy. *Sydney J. Hinds*

1741. **Roentgenographic Aspects of Complete and Incomplete Pulmonary Infarction**
M. J. SMITH. *Diseases of the Chest* [*Dis. Chest*] **23**, 532–546, May, 1953. 8 figs., 35 refs.

In this paper the author discusses the radiological aspects of pulmonary thrombo-embolism on the basis of 25 cases seen at the Santa Fe Clinic, New Mexico. He quotes figures to show the fairly high incidence of pulmonary embolism and its importance as a cause of death. In view of the more effective treatment now available, the desirability of early diagnosis is stressed, although the accuracy of radiological interpretation is still low. The pathological changes are briefly discussed, and it is pointed out that radiological changes are not usually visible until 24 hours after embolism has occurred. The appearances encountered in pulmonary embolism and thrombosis are described and illustrated. As the linear shadows in incomplete infarction may be confused with those seen in such conditions as linear atelectasis, some points to assist in differentiation are given. Mention is also made of pulmonary embolism without infarction.

[This article is worthy of study. The abstracter feels, however, that the diagnosis must, in the first instance, be based mainly on the clinical history and findings.]
Sydney J. Hinds

1742. **Roentgen Features of Pulmonary Tuberculoma**
C. C. WANG. *Radiology* [*Radiology*] **60**, 536–544, April, 1953. 7 figs., 13 refs.

The author has investigated the radiological features in 19 cases of histologically proved pulmonary tuberculoma treated at the Massachusetts General Hospital between 1938 and 1952. During the first 10 years of this period only 4 cases were discovered, the apparent recent increase in incidence being attributed largely to the advent of mass chest surveys. The patients ranged in age from 23 to 64 years, and 14 of them were asymptomatic, the lesion being detected on routine radiography.

A pulmonary tuberculoma is defined as "a localized tuberculous focus of infection in the lung, firm, encapsulated, laminated, and often with central caseation. Its thick encapsulating fibrous wall distinguishes a tuberculoma from a primary tuberculous infection." The tuberculomata in this series appeared on the radiograph as round, ovoid, or lobulated areas of increased density which might be single or multiple. They increased in size over a period of time, growth occurring in a concentric fashion. Some of them showed a tendency towards central cavitation, while in other cases calcified flecks were seen within the tumour. The lesions were

located beneath and close to the pleural surface of the lung, usually in the apical segment of an upper lobe or the upper segment of a lower lobe. Small tuberculous foci were nearly always found in the neighbourhood of tuberculomata. Tomography was very useful in differentiating a tuberculoma from a lung abscess or neoplasm. *J. Rabinowitch*

1743. **Roentgen Amniography: a Valuable and Safe Aid to Obstetrical Diagnosis**
E. M. SAVIGNAC. *Radiology* [*Radiology*] **60**, 545–558, April, 1953. 17 figs., 30 refs.

Amniography consists in radiography after the introduction into the amniotic fluid of a suitable contrast medium in order to outline the uterine cavity, and enables various aspects of maternal and foetal physiology to be studied. It was originated in 1930 by Menees and Holly for the purpose of locating the placenta, but they met with numerous difficulties and quite a few unexpected side-reactions and the method fell into disuse until it was revived by Granjon in France in 1948. Since then it has been demonstrated by numerous workers that when a suitable medium is employed the method is free of any danger to the maternal or foetal organism. Among the uses of amniography are the following. (1) Location of the placenta. (2) Location of uterine tumours and determination of their size. (3) Demonstration of any deformity of the uterus, such as a septum, which might be responsible for an abnormal presentation. (4) Demonstration of any abnormality of the foetus, such as myelocele or meningocele. (5) The sex of the foetus can occasionally be detected before birth. (6) In cases of multiple pregnancy, determination of the number of amniotic sacs present and location of placenta or placentas. (7) Establishment of foetal death. The living foetus swallows the opacified fluid, which can be easily identified in the foetal bowel and has even been demonstrated in a foetus of 6 weeks. In this way it should also be possible to detect abnormalities of the gastro-intestinal tract before birth. No evidence of activity of the foetal urinary or respiratory tract has been secured by amniography. .

The technique employed by the author at the Holy Cross Hospital, Detroit, is described. To avoid puncturing the placenta it is essential first to obtain plain radiographs in the antero-posterior and lateral positions, using a soft-tissue technique. If it is certain that the placenta does not occupy an anterior position the needle is introduced in the para-umbilical area within a radius of 2 inches (5 cm.) from the navel. Under local analgesia a 20-gauge lumbar-puncture needle with stylet inserted is introduced through the abdominal wall and peritoneum and into the uterine wall. When the needle has entered the uterine cavity the needle is seen to move to and fro because of the foetal movements abutting against the point. Then, depending upon the size of the uterus, between 40 and 60 ml. of amniotic fluid is withdrawn and the same amount of contrast material introduced into the uterus. The author uses 70% diodone, which should be warmed to body temperature. After the injection the needle is removed and the patient rolled from side to side and asked to walk about for some time. Antero-posterior, lateral, and even oblique radiographs are then taken and repeated 3 hours later to demonstrate the exact outline of the foetal soft-tissue structures and small and large bowel. The maternal bladder and its relation to the lower uterine segment can also be studied in these films, since diodone finds its way into the maternal circulation and is excreted by the kidneys, being visible in the bladder within 3 hours. The author describes 9 cases in which amniography was performed without any ill effects to mother or foetus. In one case his needle entered the placenta, but had no injurious effect. The author advocates the use of this method on a much larger scale to further our knowledge of certain aspects of maternal and foetal physiology and pathology.
J. Rabinowitch

1744. **The Radiological Investigation of the Stomach with Tetraethylammonium Bromide.** (Die Röntgenuntersuchung des Magens mit Tetraäthylammoniumbromid (Teab))
M. FÓTI. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [*Fortschr. Röntgenstr.*] **78**, 566–573, May, 1953. 8 figs.

Absence of gastric tone and peristalsis usually makes the interpretation of a barium-meal *x*-ray examination more difficult and less reliable; hence there is a tendency to use only stimulating drugs to modify the appearances. Occasionally, however, it is an advantage to be able to relax the stomach—for example, in order to distinguish between a deformity caused by active contraction of the muscularis mucosae and one due to an infiltrating scirrhous carcinoma. Although effective in only about 50% of cases, tetraethylammonium bromide (TEAB) is said to be the best agent for this purpose. It should be injected intramuscularly, as intravenous injection may lead to circulatory collapse. Some 10 to 20 minutes after the injection [dosage not stated] there is a period of increased tone which lasts for a further 10 to 20 minutes. Maximum loss of tone occurs after 40 to 50 minutes and lasts for 2 to 4 hours. Eight pairs of barium-meal films are reproduced to demonstrate the advantages which are claimed for this procedure.

[Neither with TEAB nor any other drug can scar tissue containing neoplastic cells be distinguished radiologically from scar tissue without such cells. In practice, barium-meal diagnosis is based on the recognition of familiar appearances, not on the reconstruction from first principles of the pathological process which could produce the picture seen. Most radiologists have their own particular tricks for lowering gastric tone without the use of drugs.] *Denys Jennings*

1745. **Examination of Small Intestine with Carboxymethylcellulose**
I. E. KIRSH and M. A. SPELLBERG. *Radiology* [*Radiology*] **60**, 701–707, May, 1953. 13 figs., 13 refs.

The use of simple suspensions of barium sulphate in water is liable to give rise to misleading radiological pictures of the small-intestine pattern: the normal small bowel may appear to show a " deficiency pattern " as a

result of flocculation of the barium in the presence of mucus or fat.

The authors, working at the Veterans Administration Hospital, Hines, Illinois, have employed a suspension of barium sulphate containing 2·5% by weight of sodium carboxymethylcellulose (SCMC). This protective colloid renders the suspension stable and very slow to settle. The SCMC, although chemically inert, causes a rapid transit of the meal through the small intestine. In the absence of disease, a finely serrated pattern of the contour of the small-intestine mucosa is obtained. (This is illustrated by reproductions of radiographs.)

In disease processes which alter the character of the small-intestine lumen the SCMC suspension yields good radiographs showing changes in the mucosal pattern or the calibre of the bowel. Five cases—2 of steatorrhoea and one each of tuberculous peritonitis, scleroderma involving the bowel, and regional ileitis—in which this method was used are described and illustrated.

A. M. Rackow

1746. **Experimental Oral Cholecystography with a New Contrast Medium, Teridax (Triiodoethionic Acid)**
S. MARGOLIN, I. R. STEPHENS, M. T. SPOERLEIN, A. MAKOVSKY, and G. B. BELLOFF. *Journal of the American Pharmaceutical Association* [*J. Amer. pharm. Ass.*] **42**, 476–481, Aug., 1953. 8 refs.

1747. **Phlebography in the Vertical Position and in Series.** (Phlébographie en station verticale et en série)
G. BONTE and R. CORDIER. *Journal de radiologie, d'électrologie et Archives d'électricité médicale* [*J. Radiol. Électrol.*] **34**, 1–12, 1953. 14 figs., bibliography.

The authors point out that considering the ease with which phlebography can be carried out it is surprising that more use is not made of this procedure. They regard this as being due to two factors: the difficulty of interpretation caused by the varying anatomy of the venous system and the consequent inconstancy of the appearances, and a certain lack of interest in the veins and their pathology in the past. Salient points of the anatomy and physiology of the veins of the leg are recapitulated, and the vertical position is advocated for phlebography as being the most physiological and as allowing better demonstration of the functioning of the valves of the anterior as well as the posterior veins and of the calibre of the vessels than does the horizontal. However, not all patients are able to assume this position, and its use is not advisable in cases of acute phlebitis. The chief application of the vertical technique is in the study of the sequelae of phlebitis, varicose veins, varicose ulcers, post-traumatic oedema, acrocyanosis, and similar conditions, in which it enables the superficial and deep venous systems to be demonstrated independently, the progress of recanalization to be followed in deep veins which have been thrombosed, and the state of their valves after recanalization to be checked. It is also possible to determine whether varicosities are secondary to a deep thrombosis and whether the communicating veins are allowing the passage of blood from the deep to the superficial systems, while by serial phlebography the constancy of defects may be shown and the physiology of the venous system studied.

The injection should be made into a superficial vein of the foot, when visualization of the superficial plexus of the leg will occur only in the presence of an abnormally functioning communicating vein. The patient is placed so that the leg to be examined is hanging freely, the ischium of the opposite side being supported, and the foot placed on an adjustable stool. The tourniquet should be applied about 5 cm. above the internal malleolus and just tight enough to prevent injection of the superficial plexus; the foot should be warm and pulsations of the posterior tibial artery just obliterated. An injection of 30 ml. of 50% diodone is given, followed by a similar amount of normal saline. Two films, antero-posterior and lateral, are taken at the conclusion of the injection of the opaque medium, and further pairs at intervals of 30 to 40 seconds, the final pair being taken at the conclusion of the injection of the saline. Stereoscopic films have not been found so useful as simultaneous antero-posterior and lateral films. A film of higher speed (or a faster intensifying screen) is used in the upper part of the leg to compensate for the greater density. The radiographic appearances are described in detail.

John H. L. Conway-Hughes

1748. **Principles of Vertebral Tomography.** [In English]
I. BOKSTROM. *Acta radiologica* [*Acta radiol. (Stockh.)*] Suppl. 103, 1–126, 1953. 67 figs., bibliography.

RADIOTHERAPY

1749. **Experiences with a Rapid Irradiation Technic in Oral Carcinoma**
S. RUBENFELD. *Radiology* [*Radiology*] **60**, 724–731, May, 1953. 11 figs., 5 refs.

In this paper from the Bellvue Medical Center, New York, are recorded the results of an experiment begun in 1949, in which 30 cases of advanced squamous carcinoma of the mouth and pharynx were selected for high-intensity *x*-irradiation within a total treatment time of 2 to 5 days, the object of the study being to determine the maximum safe dosage within these time limits. An *x*-ray beam with a half-value layer of 1 mm. of copper was used and several skin portals were employed, the fields in most cases being 8×10 cm. in area. The mucosal reaction was found to be the limiting factor, and the largest tumour dose found to be safe was 3,500 r, achieved in 3 to 5 consecutive days. In 6 cases in which this dose was exceeded irreversible damage to the mucosa resulted. In the other cases the mucosal reaction reached a maximum in 2 to 3 weeks and healed in about 5 weeks.

The results as regards control of the disease are presented [but not in detail], and show that 11 of the patients were surviving after 1 to 3 years, although some of them have had recurrences. [It is not stated whether these recurrences were in the treated area, nor is it clear whether the patients who died remained free from primary disease.] The author considers that in certain cases

there may be some advantage in completing the treatment rapidly in this manner before mucosal and skin reactions develop. *E. Stanley Lee*

1750. **Dissection of the Neck after Intensive Irradiation to the Neck. Its Feasibility in the Management of Cervical Metastasis from Oral Cancer**

S. G. CASTIGLIANO and C. J. ROMINGER. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **69**, 771–788, May, 1953. 8 figs., bibliography.

In the management of oral cancer cervical metastases cannot be left to go untreated while the primary is being controlled by irradiation. In 1944 the senior author, believing that irradiation alone is too conservative an approach to the control of lymph-node metastases, tested the feasibility of combining it with radical dissection. The principle of his method is to neutralize the metastatic disease temporarily by irradiation while the controllability of the primary lesion is being determined, and then to proceed to radical dissection of the neck if the primary is controlled. A dose of 6,000 to 12,000 r is delivered to the primary by peroral or external *x*-irradiation, implantation of radon seeds, or a combination of these, external irradiation being used only if absolutely necessary and then using portals only just large enough to cover the volume of tissue involved. For cervical irradiation the portals are similarly limited in size and wherever possible the same portals are used for treating both primary and secondary lesions. Each node is treated separately. Wound healing is prejudiced if large doses are given, and an area of 70 sq. cm. should not receive more than 3,000 r (in air).

In a series of 41 cases treated between 1944 and 1950 at the American Oncological Hospital, Philadelphia, the average dose delivered to the cervical metastases was 5,300 r, the highest being 11,000 r and the majority of patients receiving 3,000 to 7,000 r. In those cases in which higher doses were used the original intention had been to use radiotherapy only, but operation was later decided upon because of actively extending residual disease. The time of treatment was 3 to 5 weeks. Operation was performed when control of the primary was evident and radiation reactions had healed, the average interval being 76 days. (The ideal interval seems to be 3 to 6 weeks, though 8 to 10 weeks is acceptable; beyond this, fibrosis increases technical difficulties of the operation.) In 85% of cases little or no technical difficulty was encountered at operation. Healing time was found to depend upon the dose delivered, being unaffected by doses of less than 3,000 r. The average for the irradiated series was 38 days, 11 days longer than the average for 33 comparable cases in which neck dissection was carried out without previous irradiation. In 91% of cases positive evidence of metastatic growth was found. There were 2 postoperative deaths from heart failure. Of the irradiated group, 10 patients (32%) were alive and well 3 to 5 years after treatment, while for the non-irradiated group the figure was 3 (21%). It is concluded that the procedure is safe and may improve the end-results in cases of oral cancer with cervical metastases. *I. G. Williams*

1751. **Radiumhemmet's Method of Treatment in Hypopharyngeal Cancer**

S. HULTBERG. *British Journal of Radiology* [*Brit. J. Radiol.*] **26**, 224–233, May, 1953. 10 figs., 23 refs.

In this paper the method of radiotherapy of squamous-celled carcinoma of the hypopharynx employed at the Radiumhemmet in Stockholm is described. First the various methods of treatment available are discussed. Major surgery is considered a severe and often mutilating procedure rarely justified by the results. The various techniques of radiotherapy are then enumerated, and the importance of spreading the total dose over a certain number of days, of irradiating as small a volume of tissue as possible, and of avoiding damage to the spinal cord is stressed.

New patients are carefully assessed clinically, and the position and extent of the tumour are accurately determined by direct and radiological methods. Carcinomata arising between the laryngeal inlet and the upper part of the oesophagus just below the opening are regarded as hypopharyngeal. These are divided into an upper and a lower group, the upper border of the cricoid cartilage being taken as the line of division. The technique, which is the same for both groups, consists in irradiating two narrow crossed fields on each side of the neck measuring 3·5 to 4·0 cm. × 10 to 12 cm. One field per day is irradiated and the position of the field is checked by screen location with the patient in a special chair.

The daily dose begins with 400 r given by means of a conventional apparatus, and the treatment is continued until tumour regression has been obtained. The dose for this lies between 5,700 and 6,200 r over 28 to 32 days. In this way the skin does not receive more than 3,000 r, and proceeds only to dry, or occasionally moist, desquamation. The mucosal reaction appears in 2 to 3 weeks after the beginning of treatment and heals in about 6 to 8 weeks, though oedema sometimes persists. The importance of maintaining the patient's nourishment during treatment is stressed and a warning given that gastrostomy must be avoided. For this purpose patients should be in hospital and a special regimen followed. A late mucosal reaction occurs about 6 months after treatment; the importance of not mistaking this for a recurrence is emphasized.

If untreated, the disease is fatal in 50% of cases within 6 months. In the present series over one-third of the patients were in such poor condition that only palliative treatment was possible.

In the period 1939–47, 322 patients (119 males and 203 females) with hypopharyngeal carcinoma were treated at the Radiumhemmet. Of these, 36 have remained symptom-free for 5 years or more, the absolute cure rate being 9·3% and the relative cure rate 10·9%. A comparison of the results before and after the introduction of fluoroscopic beam direction in 1943 shows a rise in 5-year cure rate from 7 to 14·5%; cases more recently treated show a further improvement in results, so that a 5-year cure rate of 20% seems to be within reach.

[This paper should be read in the original by all interested in this subject.] *R. D. S. Rhys-Lewis*

History of Medicine

1752. **The Medical and Scientific Exploits of King James IV of Scotland**
D. GUTHRIE. *British Medical Journal* [*Brit. med. J.*] **1**, 1191–1193, May 30, 1953. 1 fig.

Many kings and queens have contributed indirectly to the advance of medical science, but few have taken an active part in scientific investigation or the practice of medicine, although Mithridates, King of Pontus, gave his name to mithridatum, the famous antidote to poisons, which he evolved for his own protection, and the " Royal Touch " for scrofula was for hundreds of years regarded as a manifestation of the healing power of anointed monarchs.

The medico-scientific exploits of King James IV of Scotland (1473–1513) were on a different plane and are probably unique in history. This king was not only a firm ruler and man of action, but was also an accomplished linguist and an amateur of science and medicine. By giving his patronage in 1495 to the then newly founded University of Aberdeen, the first British university to give instruction in medicine, and to the corporation of surgeons and barber-surgeons of Edinburgh (1505)—the body which later developed into the Royal College of Surgeons of Edinburgh—he associated himself closely with the very beginnings of systematic medical education in Scotland. His reign also saw the establishment of the first printing press at Edinburgh (1507). In the public health field he approved and reinforced various laws directed to the control of plague and syphilis and to the expulsion of beggars and vagrants. Official scavengers were employed in Edinburgh in 1499, and measures were taken to free the streets from stray dogs, cats, and pigs. The Lord High Treasurer's accounts for the period of the reign record many payments to medical men, and they also show that James himself dressed wounds, let blood, and extracted teeth, several entries revealing that the King actually paid some of his patients for the privilege of carrying out operations upon them. On one occasion he operated upon one of his own barber-surgeons, extracting two teeth.

The King also took great interest in chemistry, and granted many favours to an Italian physician and alchemist named John Damian, with whom he collaborated in experiments concerned with the transmutation of base metals into gold. In 1507 Damian attempted to fly with the aid of a pair of wings made of feathers. On launching himself from the top of a cliff he sustained a broken thigh, and this early experiment in aviation interrupted his association with the King. In another curious experiment—an attempt to determine what was the primitive language of mankind—James caused two infants to be brought up by a deaf-and-dumb nurse on the island of Inchkeith. Lindsay, the historian, reported that when the bairns came to the age of speech " some say they spak guid Hebrew. But as to my self, I know not." During the reign of James, " Siamese " twins were born in Scotland, and the King caused them to be taught to sing in parts, the one treble and the other tenor, " which was very sweet and melodious to hear". There is no doubt that the King, who met his death on the battlefield of Flodden (1513), was a man of inquiring mind, and a pioneer with views far in advance of his time.

W. J. Bishop

1753. **Medicine in the Time of Queen Elizabeth the First**
A. S. MACNALTY. *British Medical Journal* [*Brit. med. J.*] **1**, 1179–1185, May 30, 1953. 6 figs., 27 refs.

At the time of the first Elizabeth there were three classes of medical practitioners: " the physician, who was just ceasing to be an ecclesiastic; the surgeon, who had recently relinquished being a barber; and the apothecary, still associated with the grocers ". After Henry VIII had founded the College of Physicians in 1518, entry into the profession was closely regulated. The College provided medical education and held examinations, teaching being based on the doctrines of Galen. The theory of the humours governed practice. Astrology was popular, some physicians casting horoscopes to aid diagnosis. Polypharmacy was the rule in treatment, many drugs being unpleasant and based on folklore. The Letters Patent constituting the College assigned to it the duty of inspecting all drugs and destroying any defective ones found in the apothecaries' shops. This duty, which was confirmed by Statute in 1522, was discharged by the College for more than 300 years. The publication of a uniform pharmacopoeia in 1585 ushered in scientific therapeutics.

The physician of these days was a learned man, for university courses were lengthy and the degree of M.D. took fourteen years of study. Yet provision for clinical work was extremely deficient, so that the best students visited Continental schools or gained experience as Army medical officers. Many physicians were eminent in different spheres of knowledge. Some taught the classics, like John Caius, who was Professor of Greek at Padua; he collected MSS. of Celsus and Galen, corresponded with Gesner, and was a pupil and friend of Vesalius. Caius instituted the study of practical anatomy in England and was the first to teach it publicly; further, he was the co-founder of Gonville and Caius College, Cambridge, and physician successively to Edward VI, Mary, and Elizabeth. William Gilbert, another Court physician, was a great scientist and a pioneer in the field of magnetism and electricity. A physician—William Turner—was the father of English botany; and William Bullein and Thomas Penny were other medical botanists of this era. Two Fellows of the College of Physicians became headmasters, of Winchester and Eton respectively, and Thomas Campion was a poet and musician as well as a doctor. Notable

physicians were frequently involved in politics; occasionally they acted as ambassadors and sometimes were employed as secret agents for the Government. Fellows of the College attended admirals and generals on their campaigns.

There was no clear division between medicine and surgery, but as a rule physicians did not perform operations. Obstetrics was chiefly in the hands of untrained midwives, so that maternal mortality was high. Ophthalmology had its beginnings as a specialty under Elizabeth. In 1540 the Barber-Surgeons Company was formed: "The union elevated surgery to the dignity of a profession, gave it corporate and municipal privileges, set a high standard of education and qualification, and promoted the teaching of anatomy and surgery". Surgeons were not allowed to administer "inward remedies". Apothecaries belonged to the Grocers' Company and as apprentices received technical training. They compounded and dispensed medicines, were usually prosperous and reputable, and organized themselves into a professional corporation. Quacks flourished and had influential clients, despite the efforts of the College of Physicians and the Barber-Surgeons Company.

In the field of public health there were in early Tudor times men like Sir Thomas More, who grasped the principles of preventive medicine, hygiene, nutrition, and education. The Corporation of London made many regulations concerning infectious diseases, scavenging, and sanitation which were adopted under Elizabeth, when disease was widespread. The most usual illnesses among the wealthy were "surfeits" due to overeating and drinking, and gout. Scurvy, scabies, and syphilis were common; indigenous malaria persisted, especially in the Fens; leprosy, however, had been almost abolished. Measles was often mistaken for smallpox, and these two diseases, together with pulmonary tuberculosis, took a heavy toll of life. The plague had been endemic since the time of the Black Death, influenza was sometimes epidemic, and rheumatic complaints were common. Spa treatment at Buxton and Harrogate was introduced at this time.

There were few hospitals since the abolition of the monasteries. Only five metropolitan institutions survived, these being the five Royal Hospitals—St. Bartholomew's, St. Thomas's, Christ's, Bethlehem (for the insane), and Bridewell (the prison hospital). Despite this lack of hospitals medical knowledge and organization progressed under Elizabeth I, and the Queen herself offered great encouragement. *Ruth Hodgkinson*

1754. **The Faculty of Medicine at Paris, Charlatanism, and Unlicensed Medical Practices in the Later Middle Ages**
P. KIBRE. *Bulletin of the History of Medicine* [*Bull. Hist. Med.*] **27**, 1–20, Jan.–Feb., 1953. Bibliography.

The control of unauthorized physicians and the regulation of the professions ancillary to medicine were unsolved problems until very recently. Outstanding among the many attempts made by university authorities to control charlatanic practitioners and empirics were those of the University of Paris. In insisting upon registration and licence the Medical Faculty requested the help of royal, municipal, and ecclesiastical power. In 1271 and 1272 the University defined the requirements for a medical licence and outlined the duties of surgeons, apothecaries, and herbalists. However, it was found easier to make laws than to enforce them, and charlatans and empirics who were brought before the Faculty contested the legality of such action. The University claimed that it had the right given by a bishop's court regulation of the twelfth century. [But it is doubtful if the Faculty was even formed at that date, and no firm evidence exists to support the claim.] The punishment by excommunication and public denouncement did not deter others from similar practices; indeed, much support was often given by the public at the trials and appeals of empirics. At least five times during the early fourteenth century the Faculty requested the aid of the Pope (John XXII or Clement VI); as a result certain powers were given to the bishops regarding medical registration, and ecclesiastical censure fell upon those disobeying their wishes in this matter. In 1322 the University brought out ordinances relating to apothecaries and drug dealers which ordered the inspection of their shops, controlled their sale of drugs, and compelled them to have for reference the *Antidotarium* of Nicholas of Salerno. Later, these ordinances were to be strengthened by royal mandate and were also enlarged by John of France.

The attempts made by the University, the Church, and the Throne to control medical practice were never wholly successful. In the fifteenth century Henry V of England had to reaffirm the statutes of the French kings, and for long after that time the charlatan and the quack enjoyed as much worldly success as did the licentiate or the graduate. This is not surprising: the nature of man, the squabbles within the Faculty, the disputes of surgeons and barbers, and the state of medical knowledge did not make for professional cohesion. The University of Paris approached the problem early in its history and tenaciously pursued its ideal; it obtained the help of all of the authorities that influence man. It could not have done more. *T. Marmion*

1755. **Theodore Goulston, M.D., F.R.C.P. 1574–1632**
J. J. KEEVIL. *Bulletin of the History of Medicine* [*Bull. Hist. Med.*] **27**, 201–211, May–June, 1953. 21 refs.

1756. **John Arderne, the Father of English Surgery**
G. N. WEISS. *Postgraduate Medicine* [*Postgrad. Med.*] **13**, 479–486, May, 1953. 3 figs., 22 refs.

1757. **William Beaumont, Pioneer Physiologist. Centennial of his Death (1785–1853)**
F. STENN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **152**, 915–917, July 4, 1953. 2 refs.

1758. **Newman and his Medical School. The Fateful First Lustrum (1855–60)**
W. DOOLIN. *Journal of the Irish Medical Association* [*J. Irish med. Ass.*] **33**, 1–9, July, 1953.

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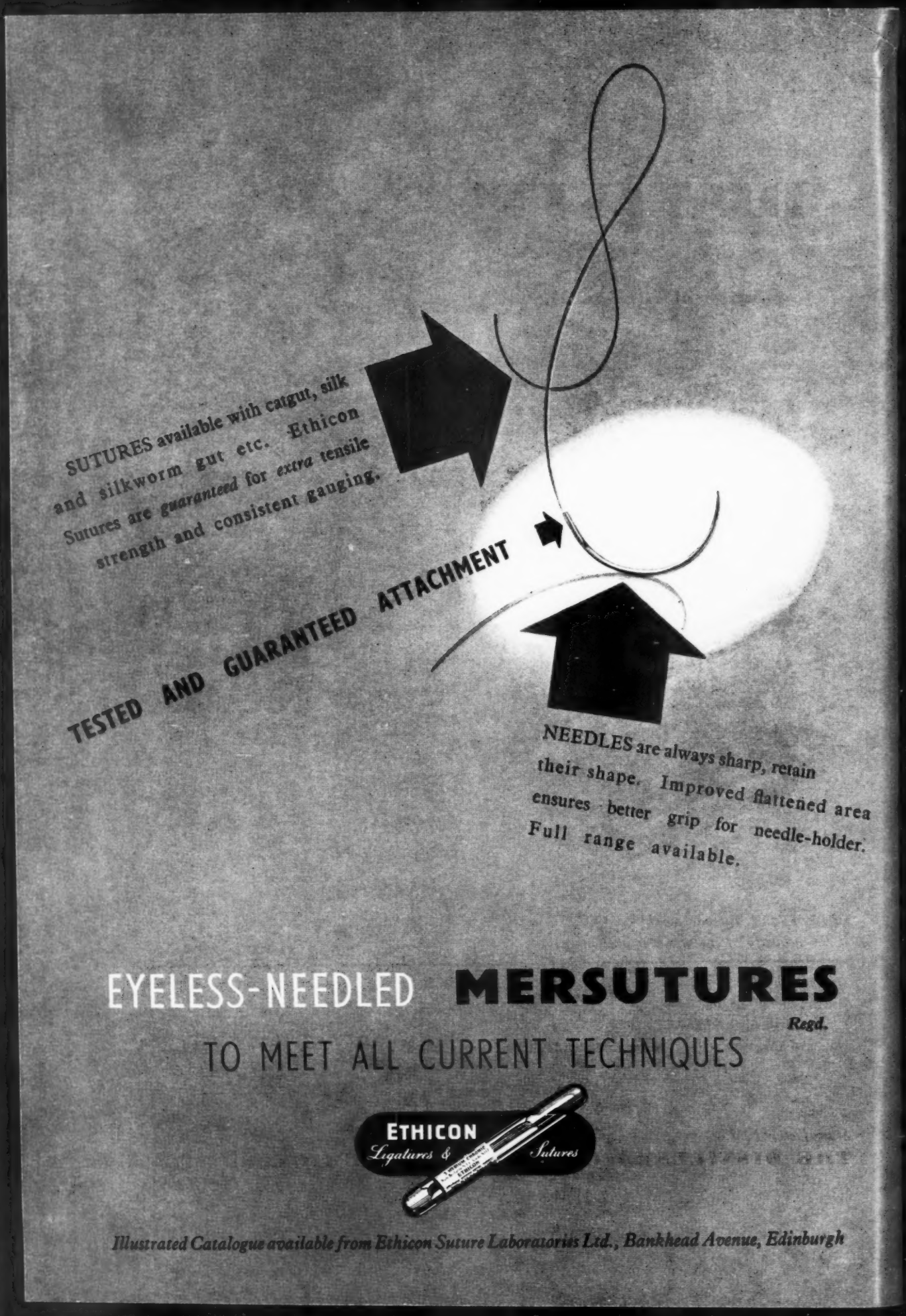
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